



University
of Glasgow

Md Isa, Nur Mahiza (2016) *Genetic resistance to nematode infection in texel*. PhD thesis.

<http://theses.gla.ac.uk/7197/>

Copyright and moral rights for this thesis are retained by the author

A copy can be downloaded for personal non-commercial research or study

This thesis cannot be reproduced or quoted extensively from without first obtaining permission in writing from the Author

The content must not be changed in any way or sold commercially in any format or medium without the formal permission of the Author

When referring to this work, full bibliographic details including the author, title, awarding institution and date of the thesis must be given

GENETIC RESISTANCE TO NEMATODE INFECTION IN TEXEL

By

NUR MAHIZA MD ISA

**Submitted in Fulfillment of the Requirements for Degree of Doctor
of Philosophy**

Institute of Biodiversity, Animal Health and Comparative Medicine

College of Medical, Veterinary and Life Science

University of Glasgow

February 2016

ABSTRACT

Nematode infection is one of the major causes of disease in young sheep. Selective breeding of genetically nematode resistant sheep is an alternative method for controlling the nematode infection. This process could be simplified if loci that account for nematode resistance can be identified. MHC is one of the candidates and several studies have confirmed the association between MHC alleles and nematode resistance. The aim of this study is to establish the role of MHC class II genes in nematode resistance in Texel sheep. Thus, it can help endorse the usefulness of the MHC class II genes as a genetic marker of nematode resistance and extend the knowledge of the mechanism of resistance against nematodes. This study has been focused on three main areas; 1) description of MHC class II gene diversity, 2) description of haplotype and linkage disequilibrium pattern at MHC class II genes and 3) the association of MHC class II genes and nematode resistance. Sequence-based typing was applied to characterise MHC class II allelic diversity in 235 Texel lambs. The haplotype and linkage disequilibrium patterns were deduced from pedigree information. Finally, the association between MHC class II haplotypes and nematode resistance (FEC and IgE activity against L3) were investigated using a MIXED model approach. MHC class IIa genes were diverse in Texel, consistent with previous studies reported in sheep. The most polymorphic locus among MHC class IIa genes was DRB1. A total of 21 distinct DR-DQ haplotypes were obtained and strong linkage disequilibrium exhibited between DR-DQ genes. There were also statistically significant associations of specific haplotypes and nematode resistance in this population. The work in this thesis confirms the likely importance of MHC genes in regulating resistance against gastrointestinal nematodes, thus supporting the use of MHC as a genetic marker of nematode resistance in selective breeding. Sequence-based typing system for MHC class IIa has been established in this study.

TABLE OF CONTENTS

Table of Contents

ABSTRACT.....	ii
TABLE OF CONTENTS.....	iii
LIST OF TABLES	vi
LIST OF FIGURES.....	x
ABBREVIATIONS.....	xiv
ACKNOWLEDGEMENT.....	xvi
AUTHOR'S DECLARATION	xviii
LIST OF PUBLICATIONS AND PRESENTATIONS.....	19
CHAPTER 1.....	20
LITERATURE REVIEW	20
1.0 General Introduction.....	20
1.1 Anthelmintic Resistance and a Desire for the Alternative Approach.....	22
1.2 Selective Breeding of Genetically Nematode Resistant Sheep.....	24
1.3. Hunting Genes Underlying Nematode Resistance.....	30
1.4 Major Histocompatibility Complex (MHC).....	32
1.5 Sheep MHC or Ovar-Mhc.....	38
1.6 Ovar-DR Genes.....	41
1.7 Ovar-DQ Genes.....	50
1.8 Thesis Objective	57
CHAPTER 2.....	58
GENERAL MATERIALS AND METHODS	58
2.1 Introduction.....	58
2.2 Previous Work	58
2.3 MHC Class II Sequence-based Typing.....	59
2.4 Sequence Data Processing and Analysis	65
2.5 Genotyping Quality Control.....	66
2.6 Submission of Alleles to the Databases	69
2.7 Statistical Analysis.....	70
2.8 Phylogenetic Analysis	71

CHAPTER 3.....	72
GENETIC DIVERSITY OF OVAR-DRB1 IN TEXEL.....	72
3.0 Summary	72
3.1 Introduction.....	73
3.2 Materials and Methods.....	74
3.3 Results	77
3.4 Discussion	84
3.5 Conclusion	85
CHAPTER 4.....	86
GENETIC DIVERSITY OF OVAR-DQA1 IN TEXEL.....	86
4.0 Summary	86
4.1 Introduction.....	87
4.2 Materials and Methods.....	87
4.3 Results	92
4.4 Discussion	100
4.5 Conclusion	102
CHAPTER 5.....	103
GENETIC DIVERSITY OF OVAR-DQA2 AND DQA2-LIKE GENES IN TEXEL	103
5.0 Summary	103
5.1 Introduction.....	104
5.2 Materials and Methods.....	105
5.3 Results	109
5.4 Discussion	120
5.5 Conclusion	121
CHAPTER 6.....	122
GENETIC DIVERSITY OF OVAR-DQB1 IN TEXEL.....	122
6.0 Summary	122
6.1 Introduction.....	123
6.2 Materials and Methods.....	124
6.3 Results	128
6.4 Discussion	136
6.5 Conclusion	137
CHAPTER 7.....	138
GENETIC DIVERSITY OF OVAR-DQB2 IN TEXEL.....	138

7.0 Summary	138
7.1 Introduction.....	139
7.2 Materials and Methods	140
7.3 Results	144
7.4 Discussion	152
7.5 Conclusion	153
CHAPTER 8.....	154
MHC CLASS IIa HAPLOTYPES AND LINKAGE DISEQUILIBRIUM IN TEXEL.....	154
8.0 Summary	154
8.1 Introduction.....	155
8.2 Materials and Methods	156
8.3 Results	157
8.4 Discussion	167
8.5 Conclusion	169
CHAPTER 9.....	170
THE ASSOCIATION OF MHC CLASS IIa AND NEMATODE RESISTANCE IN TEXEL. 170	
9.0 Summary	170
9.1 Introduction.....	171
9.2 Materials and Methods	172
9.3 Results	175
9.4 Discussion	180
9.5 Conclusion	182
CHAPTER 10	183
GENERAL DISCUSSION AND CONCLUSION	183
LIST OF APPENDICES.....	191
Appendix 1: Pedigree Record.....	191
Appendix 2: Solution and Media Preparation	194
Appendix 3: Master Mix Preparation for PCR reactions	197
Appendix 4: MHC Class II Database.....	200
Appendix 5: List of Submitted Sequences to EBI	262
Appendix 6: Amino Acid Abbreviation.....	283
Appendix 7: SAS Commands.....	284
LIST OF REFERENCES	325

LIST OF TABLES

Table 1 Differences among breeds in resistance against GIN in different continents	27
Table 2 Three groups of indicator traits for host resistance to GIN (adapted from Dominik, 2005).....	29
Table 3 Different numbers of alleles of the Ovar-DRB1 gene in multiple breeds of sheep. Adapted from Dukkupati et al. 2006a.....	45
Table 4 Association of breeds and their common alleles reported in multiple studies	47
Table 5 Association of Ovar-DRB1 with disease resistance reported in previous studies.....	49
Table 6 Association of specific of amino acid positions with resistance or susceptibility against several diseases.....	50
Table 7 Polymorphisms of the Ovar-DQA gene reported in multiple breeds of sheep	52
Table 8 Common DQA2 alleles or haplotypes found in different breeds of sheep.	53
Table 9 Haplotypes found in two DQA genes. Adapted from Hickford et al. 2007.	54
Table 10 List of associations of Ovar-DQA alleles with important diseases in sheep	56
Table 11 Polymorphisms of the expressed Ovar-DQB gene in multiple breeds of sheep.....	57
Table 12 Primers used to amplify the second exon of the MHC class II gene.....	63
Table 13 The reagent of master mix solution for sequencing reaction	64
Table 14 The temperatures and times of 'Big Dye' program in the thermo cycler	64

Table 15 Appropriate letters to be assigned to possible bases.....	65
Table 16 A table shown the example of the DQB2 alleles found from five Texel lambs. The lambs found with one allele had an * in the second column.....	66
Table 17 Haplotype obtained from six lambs from the same sire, G173. An asterisk (*) symbol shows that there was suspected error for assignment of DQB2 allele for lamb, y006. The sequence was then re-examined.	68
Table 18 Lamb haplotypes obtained from the same sire, 8t055 by the SORT BY programme. An asterisk (*) symbol showed there was an error of null for DQA1 and DQB1 genes for lamb, 100t022. The DQA1 and DQB1 retyping process were redone for that particular DNA sample (100t022).	69
Table 19 PCR primers for amplification of the second exon of the Ovar-DRB1 gene. Amplicon size includes the primer sequences.	75
Table 20 Nomenclature of Ovar-DRB1 alleles detected in Texel.....	77
Table 21 Amino acid variations in Texel in this study Vs published sheep DRB1 alleles. Amino acid positions involved in the antigen binding sites (according to Reche & Reinherz (2003) are indicated by grey background; novel amino acids found in this study are indicated in blue, while amino acids that were only found in previous studies are given in red.	81
Table 22 Ovar-DRB1 alleles and their frequencies found in Texel.....	82
Table 23 The PCR primers for amplification of the second exon of Ovar-DQA1 gene. Amplicon size includes the primer sequences.	89
Table 24 Nomenclature of the Ovar-DQA1 exon 2 detected in Texel and comparison with those previously described.....	92
Table 25 Amino acid variation in Texel in this study Vs published sheep DQA1 alleles: novel amino acids found in this study are indicated in blue. Amino acids that were only found in previous studies are given in red.....	96

Table 26 Ovar-DQA1 alleles and their frequencies found in Texel flock in this study	97
Table 27 PCR primers used for amplification the second exon of Ovar-DQA2 and Ovar-DQA2-like gene in this study.....	106
Table 28 Nomenclature of Ovar-DQA2 and DQA2-like exon 2 alleles detected in Texel.....	109
Table 29 Amino acid variations in Texel in this study Vs published sheep DQA2 and DQA2-like alleles. Amino acid positions involved in the antigen binding sites (according to Reche & Reinherz, 2003) are indicated by grey background; amino acids that were only found in previous published studies are given in red.....	113
Table 30 Ovar-DQA2 alleles and their frequencies found in Texel.....	115
Table 31 DQA Haplotypes found in Texel in this study. The two haplotypes which pose AY312392 allele are shown in bold.	119
Table 32 PCR primers used for the amplification of the second exon of Ovar-DQB1 gene in this study.....	126
Table 33 Nomenclature of Ovar-DQB1 exon 2 alleles detected in this Texel population	128
Table 34 Amino acid variation in Texel sheep in this study. Amino acid positions involved in the antigen binding sites (according to Reche & Reinherz,2003) are indicated by grey background.	132
Table 35 Ovar-DQB1 and their frequencies found in Texel in this study.....	133
Table 36 PCR primers for the amplification of the second exon of Ovar-DQB2 gene	141
Table 37 Nomenclature of Ovar-DQB2 alleles detected in Texel lambs in this study	144

Table 38 Amino acid variations in Texel sheep in this study. Amino acid positions involved in the antigen binding sites according to Reche & Reinherz (2003) are indicated by grey background.	148
Table 39 Ovar-DQB2 and their frequencies found in Texel in the present study	149
Table 40 MHC class IIa haplotypes of Texel sheep in this study.....	158
Table 41 Linkage disequilibrium between DRB1 and other MHC class IIa genes	161
Table 42 Linkage disequilibrium between DQA1 and other MHC class IIa genes (DQB1, DQA2, DQA2-like and DQB2 genes)	164
Table 43 Linkage disequilibrium between DQB1 and DQA2, DQA2-like and DQB2	165
Table 44 Linkage disequilibrium between DQA2 and DQA2-like and DQB2; DQA2-like and DQB2.....	166
Table 45 Haplotype nomenclature and their full haplotype description	173
Table 46 The description of FEC in this study	173
Table 47 The significance of effect of individual MHC class IIa haplotypes on FEC. See Table 46 for full haplotype MHC class IIa.....	176
Table 48 The significance of effect of individual MHC class IIa haplotype on anti-L3 IgE. The haplotype #p was set as a reference.....	178
Table 49 The significance of effect of MHC class IIa homozygosity on FEC and anti-L3 IgE.....	179

LIST OF FIGURES

Figure 1 The work flow of two main approaches; QTL mapping and candidate gene analysis for identifying genes associated with traits. Adapted from Venturina (2012). The key points of QTL mapping and candidate gene analysis are listed.	31
Figure 2 A schematic picture of MHC molecules and genes for class I and II; adapted from Rajalingam et al. (2010).	35
Figure 3 A schematic picture of Ovar-MHC on chromosome 20. The Ovar-MHC class II is divided into class IIa and IIb by autosome insertion. This figure is adopted from Gao et al. (2010).	39
Figure 4 Schematic picture of Ovar-Mhc class IIa loci in a Rambouillet ram; modified from Hermann-Hoesing et al. (2008a). The red and blue arrows indicate of transcription process.	41
Figure 5 Main steps for sequencing-based typing in this study	60
Figure 6 Diagrammatic representation of the second exon and immediate intronic flanking regions of the Ovar-DRB1 gene (AM884913) showing the location and direction of primers detailed in Table 19	76
Figure 7 Nucleotide sequences of the second exon of Ovar-DRB1 alleles found in Texel	79
Figure 8 Protein translation for the second exon of Ovar-DRB1 alleles found in this study. Amino acid positions have been defined according to Reche & Reinherz (2003)	80
Figure 9 A neighbor phylogenetic tree constructed from exon 2 sequences of DRB1 gene from Texel in this study. The number at the forks indicates the bootstrap confidence values and branch lengths are proportional to genetic distance.	83

Figure 10 Diagrammatic representation of the second exon and immediate flanking region of Ovar-DQA1 (M33304 sequence) showing the location and direction of primers detailed in Table 24.....	90
Figure 11 Nucleotide sequence of the second exon of Ovar-DQA1 alleles found in this study. The local allelic nomenclature is used. A dash indicates identity with the top sequence.	94
Figure 12 The distribution of polymorphisms within amino acid translations of second exon of DQA1 found in this study. Sequences within polymorphic regions: I, II and III are underline. A dash indicates identity with the top sequence, LN736359.	95
Figure 13 A neighbor phylogenetic tree constructed from exon 2 sequences of DQA1 gene from this study. The number at the forks indicates the bootstrap confidence values and branch lengths are proportional to genetic distance..	98
Figure 14 A neighbor phylogenetic tree constructed from exon 2 sequences of DQA1 gene from sheep, cattle and goats. The human DQA1 (L34082) was used as an outgroup. The number at the forks indicates the bootstrap confidence values and branch lengths are proportional to genetic distance. The yellow, red and blue symbols denote Ovar-DQA1, BoLA-DQA1 and Cahi-DQA1 respectively.	99
Figure 15 Diagrammatic representation of the second exon of Ovar-DQA2 and immediate flanking region of the Ovar-DQA2 genes showing the location of oligonucleotide primers detailed in Table 27.....	107
Figure 16 Nucleotide sequences of the second exon of Ovar-DQA2 alleles found in this study. The local allelic nomenclature is used throughout and compared with AY312375. A dot indicates identity with the top sequence.....	111
Figure 17 The distribution of polymorphisms within amino acid translations of second exon of DQA2 (including DQA2-like) found in this study. Sequences within polymorphic regions: I, II and III are underlined. A dot indicates identity with the top sequence, AY312375.	112

Figure 18 A comparison between diversity and frequencies between DQA1 and DQA2 in Texel.....	116
Figure 19 A neighbor-joining phylogenetic tree constructed from exon 2 sequences of DQA2 genes from this study. Branch lengths are proportional to genetic distance.....	117
Figure 20 A neighbor phylogenetic tree constructed from exon 2 sequences of DQA2 gene from sheep, cattle and goats. The human DQA2 (NM_020056) was used as an outgroup. Branch lengths are proportional to genetic distance. The yellow, red and blue symbols denote Ovar-DQA2 (including DQA2-like), BoLa-DQA2 and Cahi-DQA2 respectively.....	118
Figure 21 Diagramatic representation of the second exon of Ovar-DQB1 (Z28424 sequence) and immediate flanking region of the Ovar-DQB1 genes showing the location of oligonucleotide primers detailed in Table 32.	125
Figure 22 Nucleotide sequence of the second exon of Ovar-DQB1 alleles found in this study.....	130
Figure 23 The distribution of polymorphism within amino acid translation of second exon of DQB1 found in this study. A dot indicates identity with the top sequence, AH001247.....	131
Figure 24 A neighbor phylogenetic tree constructed from exon 2 sequences of DQB1 gene from this study length are proportional to genetic distance.	134
Figure 25 A neighbor phylogenetic tree constructed from exon 2 sequences of DQB1 gene from sheep, cattle and goats branch lengths are proportional to genetic distance. The blue, red and yellow symbols denote Ovar-DQB1, BoLa-DQB1 and Cahi-DQB1 respectively.....	135
Figure 26 Diagramatic representation of the second exon of Ovar-DQB2 and immediate flanking region of the Ovar-DQB2 genes showing the location of oligonucleotide primers detailed in Table 36.....	142

Figure 27 Nucleotide sequence of the second exon of Ovar-DQB2 alleles found in this study.....	146
Figure 28 The distribution of polymorphisms within amino acid translations of the second exon of DQB2 found in this study. A dot indicates identity with the top sequence, AJ238934.	147
Figure 29 A comparison between diversity and frequencies between DQB1 and DQB2 in Texel.....	150
Figure 30 A neighbor-joining phylogenetic tree constructed from exon 2 sequences of DQB1 and DQB2 genes from Texel sheep in this study. Branch lengths are proportional to genetic distance. The blue and red symbols denote Ovar-DQB1 and Ovar-DQB2 respectively.....	151
Figure 31 The association of the MHC class IIa haplotype with FEC. The most frequent haplotype, #p was set equal to zero and acted as a reference.	175
Figure 32 Association of the MHC class II haplotype with IgE activities against L3. The most frequent haplotype, #p was set equal to zero and acted as a reference.	177

ABBREVIATIONS

AADs	Amino-acetonitrile derivatives
AbMIR	antibody mediated immune response
ABS	antigen binding site
Ada	adenosine amine
ALD	asymmetric linkage disequilibrium
APC	antigen-presenting cells
BAC	bacterial artificial chromosome
BLAST	Basic Local Alignment Search Tool
BLV	bovine leukaemia virus
bp	base pairs
BZs	benzimidazoles
CMIR	cell mediated immune response
CHB	Canarian Hair Breed
DC	dendritic cells
dNTP	deoxynucleoside triphosphate
EBI	European Bioinformatics Institute
EDTA	ethylenedia-minetetraacetic acid
ELISA	enzyme linked immunosorbent assay
EU	European United
FEC	faecal egg count
GIN	gastrointestinal nematode
GIT	gastrointestinal tract
GL	globule leucocyte
GWAS	genome wide association studies
HLA	human leukocyte antigen
IEC	intestinal epithelium cell
IFN- δ	interferon gamma
Ig	immunoglobulin
IPD	Immuno Polymorphism Database
IPD-MHC	Immuno Polymorphism Database- Major Histocompatibility Complex
IUB	International Union of Biochemistry
LEV	Levamisole and other imidazothiazoles
L1	larvae 1
L2	larvae 2

L3	larvae 3
L4	larvae 4
L5	larvae 5
HLA	human leukocyte antigen
MEGA	Molecular Evolutionary Genetics Analysis
MHC	major histocompatibility complex
MLs	macrocyclic lactones
NCBI	National Center for Biotechnology Information
NC-IUB	Nomenclature Committee of the International Union of Biochemistry
OLA	ovine lymphocyte antigen
OPA	Ovine pulmonary adenocarcinoma
OPPV	Ovine progressive pneumonia virus
ORF	open reading frame
OVAR	<i>Ovis aries</i>
PBS	phosphate-buffered saline
PCV	packed cell volume
PRR	pattern recognition receptor
QTL	quantitative trait loci
RFLP	Restriction fragment length polymorphism
RHM	Regional heritability mapping
RSCA	Reference-Strand-mediated Conformation Analysis
RT-PCR	Reverse Transcriptase- Polymerase Chain Reaction
SNP	Single nucleotide polymorphism
SSCP	Single-strand conformation polymorphism
STR	Simple tandem repeat
TBS	Tris-borate-EDTA
Th	T helper
TLRs	Toll like receptors
TSLP	Thymic stromal lymphopoietin
UK	United Kingdom
WAAVP	World Association for the Advancement of Veterinary Parasitology
3-D	three dimensional
α	alpha
β	beta

ACKNOWLEDGEMENT

All praises to Allah, I offer You my humble thanks and gratitude for giving me the strength and patient in completing this PhD thesis.

Working on the PhD has been a wonderful and often great challenge. I am forever thankful to many individuals who in one way or another contributed and extended their valuable assistance in the preparation and completion of this study.

Ministry of Higher Education Malaysia (MOHE) and University Putra Malaysia (UPM) for providing the financial support that allowed this PhD journey to become a reality.

Professor Michael J. Stear, my principal supervisor who has guided and supported me throughout this journey. His excellent advices and constructive criticisms in thesis works deserve special recognition.

Professor David P. Eckersall, my second supervisor; who has had a very positive influence on me from the very beginning of my PhD. Lessons he taught me will last a lifetime.

Mr. Chris McComb, Mrs. Marge Robinson, Mrs. Nicola Brady, Mrs. Denice Ritchie, Dr. Karen Fairlie-Clarke, Ms. Abby Stear, Dr Shahrom Salisi and Mrs. Caline Koh for constantly helping me in the lab.

Dr. Josie Beeley, Dr. Ibrahim Abu Anka, Dr. Intan Sameha and Mr. Latif Muti who has offered much their time in proof reading my draft thesis.

Mr. Mohd Sufri Mohammad Hamka, my husband, words are not enough to express my gratitude to you. This thesis would not have been completed without your support.

My love, **Muhammad Umair Darwisy**, thank you darling for giving me happiness. You are the reason why this journey bearable.

Mr. Haji Md Isa bin Ja'afar and **Mrs. Hajjah Rohani Abdul Jamal**, my beloved parents, both you are always my source of motivation, all my life.

Mrs. Nur Mardhati Md Isa, my only sister, my best friend, whose encouragement was never ending.

Mr. Mohd Mahizam Md Isa, **Mr. Mohd Ihsan Md Isa**, **Mr. Mohd Iyad Sufi Md Isa**, **Mr. Mohd Afiq Abdul Ghani**, **Mrs Nur Fasihah Othman** and **Mrs. Siti Suhaiziah** who always express enough gratitude of for all love and supports.

Special thanks to **Mr. Irwan Dahnil** for helping and supporting me during my finishing stage. I also wish to thank, my teacher and idol, **Professor Dr. Rehana Abdullah Sani** for her advices and non-stop moral support.

Dr. Nikhbakth, **Dr. Bishop** and **Dr. Schwaiger**, who have contribute their data to to this thesis.

Claire Hevin Zaccaron, **Beatrice Beucler**, **Dagmara Kowalska**, **Marta**, **Dorothea**, **Alexandra Muttocks**, **Jamie Orr**, **Jamie McFadzean** and **Adam Russell**; who helps for sequencing process and became my buddies in the lab.

Thorsten, **Joaquin**, **Fuhmi**, **Eilidh**, **Mark Braceland** and **Dr. Hayyan**; who sharing their knowledge and opinions. These great people have always been fantastic and enthusiastic especially when dealing with my endless enquiries about various things, for which my mere expression of thanks does not suffice.

I extend my apologies to everyone whom I have not mentioned in this thesis. And of course, for any errors or inadequacies that may remain in this work, the responsibility is entirely my own.

NUR MAHIZA MD ISA, February 2016.

AUTHOR'S DECLARATION

I declare that the work presented in this thesis is original, was carried out solely by the author or with due acknowledgement and has not been presented for the award of a degree at any other University.

Nur Mahiza Md Isa, February 2016.

LIST OF PUBLICATIONS AND PRESENTATIONS

- 2015** **25th International Conference of the World Association for the Advancement of Veterinary Parasitology**
- The genetic architecture of the Major Histocompatibility Complex (MHC) class II in sheep and its role in resistance to nematode infection, Liverpool, UK
-
- 2015** **British Society for Parasitology Spring Meeting 2015**
- Ovar-MHC class II haplotypes and Nematode Resistance in Sheep, Liverpool, UK
-
- 2014** **British Society for Parasitology Spring Meeting 2014**
- MHC Class II DQA1 Diversity and Nematode Resistance in Scottish Blackface, Cambridge, UK
-
- 2013** **24th International Conference of the World Association for the Advancement of Veterinary Parasitology**
- Variation and High Linkage Disequilibrium among Ovar-DRB1, DQA1 and DQB1 loci in Scottish Blackface, Perth, Australia
-
- 2013** **67th Association for Veterinary Teaching and Research Work (AVTRW)**
- MHC class II DQA1 Diversity and Nematode Resistance in Scottish Blackface, Nottingham, UK

CHAPTER 1

LITERATURE REVIEW

1.0 General Introduction

The United Kingdom (UK) is the leading sheep producer among European Union (EU) countries as well as being one of the most important sheep producers in the world. In 2012, the UK was recorded as having the largest sheep population in the EU with approximately 32.2 million animals, including 15.2 million breeding females (National Sheep Association, 2014). In terms of sheep meat exportation, UK is ranked the third largest after New Zealand and Australia, accounting for approximately 10% of the global sheep exports in the same year (Vipond, 2010). Thus, the economic importance of the sheep industry for the UK is undeniable.

There is no doubt that gastrointestinal nematodes (GIN) adversely affect profitability of the livestock industries in the UK. To illustrate this, Nieuwhof & Bishop (2005) reported the impact of GIN with an estimated loss of £100 million per annum. Briefly, the losses derived from three primary sources, the loss associated with performance of the animals, treatment costs and prophylaxis measures. They also reported that loss due to performance was considered the key contributor, which made up over three-quarters of the total cost.

The loss due to performance in sheep can be segregated into four contributing factors (reviewed by Nieuwhof & Bishop 2005). One of them is due to a reduction of live-weight gain and alteration in body composition. The reduction in live-weight gain alone resulted in losses totalling £64 million. Secondly, there are also losses due to diminution in production of wool and milk. This is a consequence of loss of appetite among infected animals, causing a net movement of amino acid nitrogen to the liver and gastrointestinal tract (GIT) from muscle and skin, hence leading to the reduction in milk and wool production. Thirdly, infected sheep eventually lose the ability to reproduce; this is as a consequence that the host needs to pay for immune function. Finally, there is mortality or low survivability, observed especially in heavily parasitized ruminants.

Major losses in economic profit together with concern for animal welfare have initiated various approaches in controlling GIN problems. The traditional method of using anthelmintic drugs is still popular option and majority farmers still rely heavily on these (Ellis et al. 2014). This usage of anthelmintic drugs has led to rapidly evolving resistance to multiple anthelmintic drugs (Papadopoulos et al. 2012). In addition, the anxiety of maintaining 'green' and ecological environments from society has pressured the search for alternative approaches (Waller & Thamsborg 2004). Alternative approaches for nematode control in ruminants have been researched and some approaches are promising (Chandrawathani et al. 2002; Karlsson & Greeff, 2006). One promising approach is to breed genetically nematode resistant animals (Stear et al. 2006).

The identification of genetically resistant animals could be facilitated if the loci which regulate resistance against GIN were known (Stear et al. 2007). In addition, it would aid understanding of the mechanism of the host immune system against parasites. The major histocompatibility complex (MHC) allele was found to be associated with nematode resistance in numerous studies (Schwaiger et al. 1995; Stear et al. 1996; Paterson et al. 1998; Sayers et al. 2005b; Stear et al. 2005; Keane et al. 2005; 2007; Castillo et al. 2011; Valilou et al. 2015). However, the question remains as to whether the observed effect was a direct or indirect influence (Stear et al. 2007; Keane et al. 2007). Identifying the causative mutations remains to be determined (Stear et al. 2009).

In this introductory chapter, the primary goal is to provide an in-depth understanding of these five major areas:

- a) Anthelmintic drug resistance and existing approaches for nematode control in the sheep industry with emphasis on boosting of the host immune response.
- b) Selective breeding of genetically nematode resistant sheep.
- c) Genes underlying nematode resistance.
- d) MHC structure and characterisation.

- e) Existing and current knowledge on Ovar-MHC (Ovar-DR and DQ) genes and their association with disease resistance.

1.1 Anthelmintic Resistance and a Desire for the Alternative Approach

Sheep are infected with a wide array of GIN (Miller & Horohov, 2006). Based on predilection sites, these parasitic worms have been grouped into abomasum nematodes; *Teladorsagia circumcincta* (brown stomach worm) and *Haemonchus contortus* (barber pole worm), small intestine nematodes; *Cooperia* spp. (cooper's worm), *Nematodirus* spp. (threadneckworm), *Trichostrongylus colubriformis* (bankrupt worm) and large intestine nematodes; *Oesophagostomum* spp. (nodular worm) (Urquhart et al. 1987). GIN such as *T. circumcincta*, *T. vitrinus*, *T. axei*, *Nematodirus battus*, *Nematodirus filicolis*, *Nematodirus spathiger* and *Cooperia* spp. are prevalent taxa that affect sheep (Stear et al. 1998).

The most significant strongylid nematode in the UK is *T. circumcincta* (Stear et al. 1998; Stear et al. 2005; Venturina et al. 2013). Although *T. circumcincta* poses low fecundity compared with other members of the trichostrongylid nematodes (0-350 eggs/female/day) (Stear & Bishop 1999), they are dominant and successful parasites in temperate areas of the world (Stear et al. 2011). To illustrate this point, more than 80% of adult GIN were identified as *T. circumcincta* in the necropsy of over 500 sheep (Stear et al. 1997). The greater survivability of *T. circumcincta* is probably best explained by their survival strategy compared with other GIN (Stear et al. 1997).

Traditionally, anthelmintic drugs are being used by farmers globally to control GIN problems. Until today, they still rely heavily on these drugs (Ellis et al. 2014). The use of anthelmintic drugs to control nematodes started with the launch of phenothiazine in the late 1930s (Sayers & Sweeney 2007). Three main classes of chemical drugs are available for control of sheep GIN namely; benzimidazoles (BZs); levamisole and other imidazothiazoles (LEV) and macrocyclic lactones (MLs). Amino-acetonitrile derivatives (AADs) and derquantel-abamectin are the latest class of drugs which is suitable for a variety of species of livestock nematodes (Kaminsky et al. 2008; Little et al. 2010). The use of anthelmintic drugs is still popular because they are easy and handy to use and cost-effective (Ellis et al. 2014). Sargison (2011) argued that efforts to control nematodes are bound to be unsuccessful without the use of anthelmintic drugs.

The global issue in the usage of anthelmintic drugs is the rapidly evolving resistance to anthelmintic drugs in GIN of sheep and that resistance is a heritable trait (reviewed by Kaplan, 2004). The first suspicion of anthelmintic drug resistance was reported by Drudge et al. (1957), which was related to phenothiazine resistance. In temperate regions, the first indication of anthelmintic resistance in farms is usually the failure of lambs to reach finished weights by late autumn, scouring and mortality due to GIN infection despite having been given anthelmintic drugs (Sargison, 2011).

In the UK, anthelmintic drug resistance has been well studied (Sargison et al. 2007; Taylor et al. 2009; Mitchell et al. 2010). The level of drug resistance to BZs is higher as compared to LEV and ML in the UK (Taylor et al. 2009). In addition, the three classes of drugs mentioned were associated with multidrug resistance (Sargison et al. 2007). Taylor et al. (2009) found that 97% of sheep farms incorporated in their study had populations containing alleles conferring resistance to BZs. Thus, it is undeniable that anthelmintic drug resistance is a major problem in the UK and thus a search for an alternative approach is mandatory. It is also aggravated by the fact that the problems of acquired resistance to anthelmintic parasite is expected to continue (Mitrevae et al. 2007).

Alternative approaches were proposed to replace the use of anthelmintic drugs with a different strategy. These have been comprehensively reviewed by authors such as Stear et al. (2006), Sayers & Sweeney (2007) and Torres-Acosta & Hoste (2008). Each of the alternative approaches has advantages and disadvantages, and the choice of implementation should consider conditions on farms and local epidemiology (Torres-Acosta & Hoste 2008). Collectively, three main principles are applied in the alternative approach for GIN control. Firstly, to minimize the contact between host and infective larvae through grazing management. Secondly, to control the parasite with alternative treatment such as natural plants and minerals. Lastly, to boost host immunity (Torres-Acosta & Hoste 2008). In this chapter, it is not intended to review all possible alternative approaches, but an approach based on boosting the host immune response by breeding nematode resistant sheep will be discussed and enhanced with up to date information.

1.2 Selective Breeding of Genetically Nematode Resistant Sheep

Selective breeding for disease resistance is a common practice in the livestock industry. The evidence has been extensively reviewed (Bishop et al. 2011). Stear et al. (2001) asserted that breeding for disease resistance is not only sustainable; it is also a feasible and desirable approach. One example of selective breeding implemented in the sheep industry is breeding for nematode resistance. In richer countries such as Australia and New Zealand, sheep breeding companies have been breeding for nematode resistance for a long time (Gray, 1997).

When considering nematode resistance, firstly we require a definition of 'resistance'. Resistance is defined as the ability of the host to carry a reduced parasite burden (Stear et al. 2001). Sheep are classified as resistant animals if three consequences are observed after parasite entry into the host body: the parasite is unable to establish infection, even if they can establish infection they are incapable of completing their life cycle, and if they manage to become established and complete their life cycle but they are rejected from host (Stear & Wakelin 1998). Even though the exact and precise mechanism of resistance is not entirely understood for all GIN, the general principle applied is an increase in host resistance associated with a better immune resistance against parasite (Stear et al. 1999).

Breeding of genetically resistant sheep is a better option compared to other alternative methods. Firstly, the effect is a permanent solution demanding no extra resources and is also an inexpensive method (Waller & Thamsborg 2004). Secondly, selecting resistant animals is not only able to slow down the development of anthelmintic resistance, but is meeting the demand for drug free residues in meat for customers (Stear et al. 2007). Thirdly, selection of resistance against one nematode also enhances resistance to other GIN (Gruner et al. 2004). Fourthly, a strong favourable genetic correlation between resistance (FEC) and growth rate (Bishop et al. 1996) and the heritability of nematode resistance is one-third (Bishop et al. 1996) suggesting that the breeding of nematode resistance is feasible (Stear et al. 2001). In addition to that, breeding nematode resistant sheep has been shown to have positive outcomes (Karlsson & Greeff 2006; Kemper et al. 2010). Karlsson & Greeff (2012) suggested that breeding for nematode resistance is the ultimate 'instrument' for controlling parasites in the long term.

Substantial debate exists as to whether selection should be based on resistance or resilience. Resilience is sometimes called tolerance (Kelly et al. 2013). In contrast to resistance, 'resilience' is when the host infected by the pathogen suffers minimal adverse effects and the animal is able to sustain a relatively undepressed production level during parasite infection (Kelly et al. 2013). Furthermore, there was evidence that there is negative genetic correlation between resistance and resilience (Rashidi et al. 2013). The main benefit of resistance compared with resilience is to reduce contamination of larvae in the field, thus other non-resilient sheep have a lower risk of parasite challenge (McManus et al. 2014). Perhaps, selection of resistance in conjunction with other methods is the more attractive way to control nematodes (Stear et al. 2007).

1.2.1 Selection among breeds

There are more than one thousand different breeds of sheep in the world, and evidence of genetic variation in nematode resistance among breeds is well documented in different continents (**Table 1**).

Differences in susceptibility among breeds have been observed especially towards the blood feeder, *H. contortus*. In the African continent, breeds such Red Masai, Sabi, Djallonke, Dorper and Menz (Mugambi et al. 1996; Goossens et al. 2000; Rege et al. 2002; Matika et al. 2003) have been shown to be relatively resistant to *H. contortus*. Similarly, in Asia, breeds such Sumatra, Garole, Lohi and Local Kashmiri crosses (Nimbkar et al. 2000; Romjali et al. 2000; Tariq et al. 2008; Saddiqi et al. 2010) are also relatively resistant to same parasite. While, in the American continent, the St Croix, Blackbelly, Katahdin, Gulf Coast Native, Santa Ines and Criollo (Burke & Miller 2002; Amarante et al. 2005; Miller et al. 2006; Amarante et al. 2009; MacKinnon et al. 2009; Alba-Hurtado et al. 2010) were also established to be relatively resistant to *H. contortus*. Studies in European countries provide evidence that Canarian Hair Breed (CHB), Merinoland and Texel breed (Gruner et al. 2003; Good et al. 2006; Hielscher et al. 2006; González et al. 2008) are also relatively resistant to *H. contortus*. The differences in susceptibility between breeds toward *H. contortus* are obviously prominent in different geographical regions of the world. However, the fact that some of the breeds come from different countries should be taken into account. For example,

Criollo sheep which were brought to Mexico during colonial time (Alba-Hurtado et al. 2010).

Table 1 Differences among breeds in resistance against GIN in different continents

Region	Relatively Resistant	Relatively Susceptible	Reference
Africa	Djallonke	Djallonke-Sahelian	Goossens et al. 2000
	Menz	Horro	Rege et al. 2002
	Red Masai	Dorper	Mugambi et al. 1996
	Sabi	Dorper	Matika et al. 2003
Asia	Garole	Decanni, Bannur	Nimbkar et al. 2000
	Java Fat-tail x Sumatra	Sumatra	Romjali et al. 2000
	Lohi	Kachhi, Thalli	Saddiqi et al. 2010
	Local Kashmiri	Crossbred Kashmir Merino	Tariq et al. 2008
	St-Croix x Sumatra	Sumatra	Romjali et al. 2000
North America	Dorper, Katahdin, St-Croix	Hampshire, Suffolk	Burke & Miller 2002
	Florida Native	Rambouillet	Amarante et al. 2005
	Gulf Coast Native	Suffolk	Miller et al. 2006
South America	Canarian Hair	Canaria	González et al.2008
	Criollo	Suffolk	Alba-Hurtado et al. 2010
	Santa Ines	Ile de France and Suffolk	Amarante et al. 2009
European	Blackbelly	Romane	Gruner et al. 2003
	Merinoland	Rhoen	Hielscher et al. 2006
	Texel	Suffolk	Good et al. 2006

The evidence for variation in genetic resistance among breeds to *T. circumcincta* is supported by previous studies. An early investigation on 29 sheep of five different breeds suggested differences in susceptibility to *T. circumcincta* (Stewart & Miller 1938). Another research group has implied that the purebred Texel breed is more resistant than sheep of the purebred Suffolk breed to this organism in a natural challenge (Good et al. 2006) and experimental infection (Ahmed et al. 2015).

1.2.2 Selection within Breeds

Farmers can substitute susceptible breeds with resistant breeds in GIN endemic areas (Stear et al. 2006). Even though the use of a resistant breed that has already been adapted is simple, it comes with obstacles such as unfavourable response from sheep farmers and good performance in economic traits of the nematode susceptible breeds (Stear et al. 2006). Substitution of breeds is not a viable option in all farms. Thus, selection within a breed is to be adopted (Stear et al. 2006). Generally, if a breeder needs to set up a selection scheme, they are required to identify a selection objective, followed by a selection criterion and a selection index (Nicholas, 1987). In the big livestock producer countries such as Australia and New Zealand, nematode resistance is one of components of the selection objective in some commercial farms (Stear et al. 2002).

1.2.3 What Traits Reflect Resistance to GIN?

Resistance to GIN is clearly a complex physiological characteristic (Dominik, 2005) and nematode resistance status can be described in terms of parasitological, immunological and/or pathological parameters (see **Table 2**). Low FEC is usually regarded as a sign of a nematode resistant animal. Typically, higher abilities of immunological and pathological responses are associated with low FEC, thus immunological and pathological parameters become the indicator of resistance. A review on parameters which reflect nematode resistance in the context of the small ruminant has been well provided by Saddiqi et al. (2012).

Table 2 Three groups of indicator traits for host resistance to GIN (adapted from Dominik, 2005)

Indicator Traits		
Parasitology	Immunology	Pathology
FEC, number of adult, length of adult	Serum (IgG1, IgA, IgE), peripheral eosinophil, mast cells, eosinophils, goblet cells	Pepsinogen concentration, albumin concentration, fructosamine concentration, PCV, dag score, faecal consistency

1.2.3.1 FEC as a Phenotypic Marker for Nematode Resistance: Advantages and Disadvantages

FEC is a chosen parameter reflecting nematode resistance because: i) simple to measure (Raadsma 1998) and highly repeatable (Stear et al. 1995b), ii) the heritability of the single FEC ranging from 0.2 to 0.4, and this value is similar to heritability of milk production in dairy cattle (Bishop et al. 1996; Morris et al. 2000), iii) selection of low FEC is a part of breeding programmes and has been proven to be successful in Australia and New Zealand, without any adverse genetic correlation with important economical traits (Karlsson & Greeff, 2006). The test has been promoted in small ruminant production (Preston et al. 2014) and iv) a computer simulation model has shown that selection of resistance based on FEC is promising and should be useful for another 20 years (Kemper et al. 2013).

Even though FEC was successful in determining resistance animals, the drawbacks seemed to overshadow the advantages. The drawbacks of FEC include time-consuming and labour intensive processes and most importantly, the animal needs to have encountered the parasitic challenge. This compromises the health and welfare of the animal. In addition, with the less fecund GIN such *T. circumcincta*, the number of eggs and worm burden are poorly correlated (Lee et al. 2011). The fact that the density-dependent relationship contributes to a low FEC even though the animal is heavily infected is another important concern (Bishop & Stear 2000).

1.2.3.2 Other Potential Phenotypic Markers?

Other phenotypic pathological or immunological parameters could potentially also be used as a marker or supplementary markers for nematode resistance (Saddiqi et al. 2012). However, the markers could not be broadly applied to all nematodes species (Stear et al. 2007). A trait such as packed cell volume (PCV) by FAMACHA® was only important with blood feeder nematodes, while pepsinogen may be appropriate for only abomasal parasites like *T. circumcincta*. For parameters to be applied, several considerations must be taken into account. The heritability of trait, is one of major determinant as it would affect the selection of response (Beh & Maddox, 1996). Besides heritability, a correlation with other production traits and cost of testing are important criteria for trait selection of nematode resistance (Preston et al. 2014). Even though there are several possible phenotypic markers that are good quality and potentially useful, problems such as uncertain exposure to parasite and variation of climatic conditions hinder the use of phenotypic markers to be used widely (Hunt et al. 2008). With these constraints, genetic markers have been suggested for identifying nematode resistance animal.

1.2.3.3 Genetic Markers for Nematode Resistance?

Genetic markers or DNA-based tests have been proposed as a marker for nematode resistance. Genetic markers were introduced in the 1970s, with the aim to detect quantitative trait loci (QTL) or loci that control genetic variation (Gibson & Bishop 2005). Genetic markers can avoid problems encountered when phenotypic marker is not efficient anymore due to absent of parasite challenge in field (Hunt et al. 2008). Many studies attempted to find QTL for nematode resistance in sheep and will be elaborated further in the next section.

1.3. Hunting Genes Underlying Nematode Resistance

The identification of genes or QTL, which code for control nematode resistance, could aid selective breeding (Stear et al. 2007). Two methods are used in genetics to identify the gene associated nematode resistance; these include QTL mapping and candidate gene analysis. The main key difference between the two methods is illustrated in **Figure 1**. Both have advantages and disadvantages, and implementation depends on

the specific aims and available resources (Venturina et al. 2013). The important difference between the two approaches is that candidate gene analysis is able to detect a gene with a small effect (Venturina et al. 2013). Candidate gene analysis shall be focussed on the next subsection as this topic is relevant in this study.

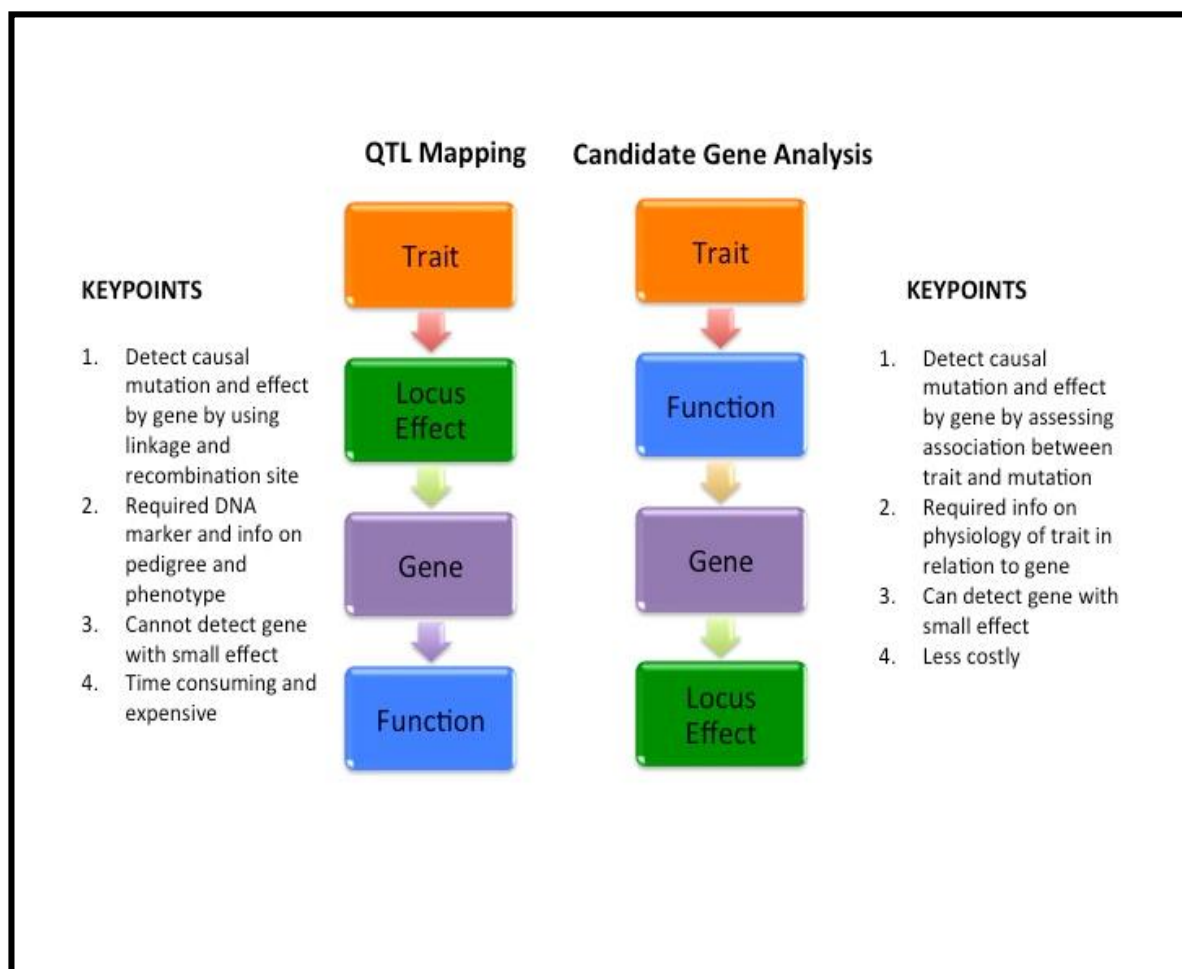


Figure 1 The work flow of two main approaches; QTL mapping and candidate gene analysis for identifying genes associated with traits. Adapted from Venturina (2012). The key points of QTL mapping and candidate gene analysis are listed.

1.3.1 Candidate Gene Analysis

Testing or analysis of candidate genes is useful approach when there is prior knowledge of the genes or pathways in biological, physiological and functional of disease in question. The aim of the candidate gene analysis is to determine the relation between a particular phenotypic trait and mutation in a given gene. As illustrated in **Figure 1**, the advantage of candidate gene analysis compared to QTL mapping is powerful due to its ability to detect trait loci with even a small effect. From thousands of genes, two important genes have been used for candidate gene analysis for identifying QTL underlying resistance to nematodes, predominantly *T. circumcincta*. These include interferon gamma (Sayers et al. 2005a) and MHC genes (Schwaiger et al. 1995; Paterson et al. 1998; Sayers et al. 2005b; Stear et al. 2005; Stear et al. 2007).

The biological and functional explanation of interferon gamma having been identified in association studies is that interferon gamma influences the variation in cytokines (Stear et al. 2007). The interferon gamma gene has been associated with susceptibility of animals to nematode infections. Abuargob (2006) study has concluded that the interferon gamma F allele locus is associated with dominant susceptibility in young male sheep. Crawford and others performed investigations on free-living Soay sheep, and they found that the interferon gamma allele (o (IFN)- γ 459) allele was associated with reduced FEC in lambs and yearlings (Crawford et al. 2001). While the work of Davies and others has identified the chromosome 3 as being associated with IgA activity and is very close in the interferon gamma locus (Davies et al. 2006).

On the other hand, MHC influences antigen presentation and the quality of immune response (Stear et al. 2007). The polymorphic MHC class II shows heterozygote advantage resistance to nematode infection (Stear et al. 2005). In particular, the G2 or Ovar-DRB1*1101 allele is associated with nematode resistance. The MHC and its association with nematode resistance will be elaborated later.

1.4 Major Histocompatibility Complex (MHC)

MHC has become one of the most widely studied regions in higher animal genomes in the fields of immunology, genetics and evolutionary biology (Horton et al. 2004). The discovery of MHC was initially from genetic studies of transplant incompatibility

(Gorer, 1934), from its name derived. The MHC encodes glycoproteins that present antigen peptides on the cell surface to T cells and thus create histocompatibility or “self” identification, for the immune response (Gorer et al. 1948). Tissue transplantation experiments first discovered an MHC in mice, the H-2 complex, and later, Dausset (1958) working on human leukocyte antigens discovered the Human Leucocyte Antigen system or HLA.

MHC molecules play a central role in the adaptive immune system (Warner et al. 1987). The activation and differentiation of the T cell is prerequisite the interaction of MHC molecules present on antigen cells and T cell receptors (Ting et al. 2002). It is well known that MHC molecules on cell membrane bind to parasite peptides and display them on the cell surface, where they are later recognized by T cell receptors. The difference in resistance to the parasite could occur because of the failure of antigen presentation by MHC molecules to T cells (Stear & Wakelin 1998). It has been known that specific HLA alleles may significantly change the presentation of antigen derived peptides to T cells resulting in different outcomes in immunity (Racioppi et al. 1991). In order to further the understand the MHC, the review presented in the following section will focus on the MHC genes and their molecular structure. In addition, the essential basic concepts in the MHC area will also be discussed.

1.4.1 Organization of MHC

MHC is an organised cluster of tightly linked genes. Within the human MHC or HLA, nearly 10-20% of the genes are associated with the immune system (Trowsdale 2011). In humans, the MHC gene is located at the 6p21.3 band on chromosome 6 and contains about 224 genes spanning approximately 4Mbp equal to 0.1% of the human genome (Trowsdale, 2011). MHC is divided into three parts on the short arm of chromosome 6: MHC class I (telomeric class), II (centromeric class) and III (central class). HLA-A, -B and -C are located in MHC class I (refer to HLA class I) and HLA-DRB1, HLA-DQB1 or HLA-DPB1 are found in MHC class II (refer to HLA class II). The MHC class III is composed of immune-related genes (eg: TNF) and non-immunological genes and pseudogenes (Kelley et al. 2005). The class I has been identified as a paralogous gene (diverged after a duplication event) , while the class II and class III regions are orthologous genes (diverged after a speciation event) (Dukkipati et al. 2006b).

1.4.2 Three-dimensional Structure of the MHC Molecule

MHC molecules are glycoproteins which are important for the capture of peptides from antigens on cell surface and their presentation to T cells. Therefore, there has been considerable interest to study the structure of MHC molecules especially the antigen-binding site. The three-dimensional (3-D) structures of MHC molecules have been revealed by Bjorkman et al. (1987) and Brown et al. (1993). They used X-ray crystallography which revealed the site for antigen-binding and contact with the T cell receptor.

Both class I and II molecules consist of alpha (α) and beta (β) glycoprotein chains (**Figure 2**). The class I molecules (encoded by HLA-A, -B, or -C genes) consist of multiple domains including α 1, α 2 and α 3. The α 1 and α 2 are distal domain and α 3 is proximal to the cell surface membrane. The α 1 and α 2 domains form the antigen binding cleft of class I molecule (Bjorkman et al. 1987). As illustrated in **Figure 2**, Class I genes contain eight exons, and only exons 2 and 3 of Class I genes are important for encoding the polymorphic antigen-binding domains (Rajalingam et al. 2010).

The Class II molecules (α encoded by DRA, DQA1 or DPA1 and β encoded by DRB1, DQB1 or DPB1) consist of two external domains: α 1 and β 1 (distal domain), α 2 and β 2 (proximal domain) (**Figure 2**). It is well known that the distal domains α 1 and β 1 form the antigen-binding cleft (Brown et al. 1988). The class II genes contain up to seven exons and only exon 2 of Class II genes encodes the antigen binding site (Rajalingam et al. 2010).

The class I and II molecules differ in their expression and function (Dukkipati et al. 2006a). The class I molecules are expressed on all nucleated cells and they present exogenous peptides to CD8+ T lymphocytes. Class II molecules, on the other hand are expressed on antigen presenting cells (APC). Example of APC includes dendritic cells, macrophages, B cells and the thymic epithelium.

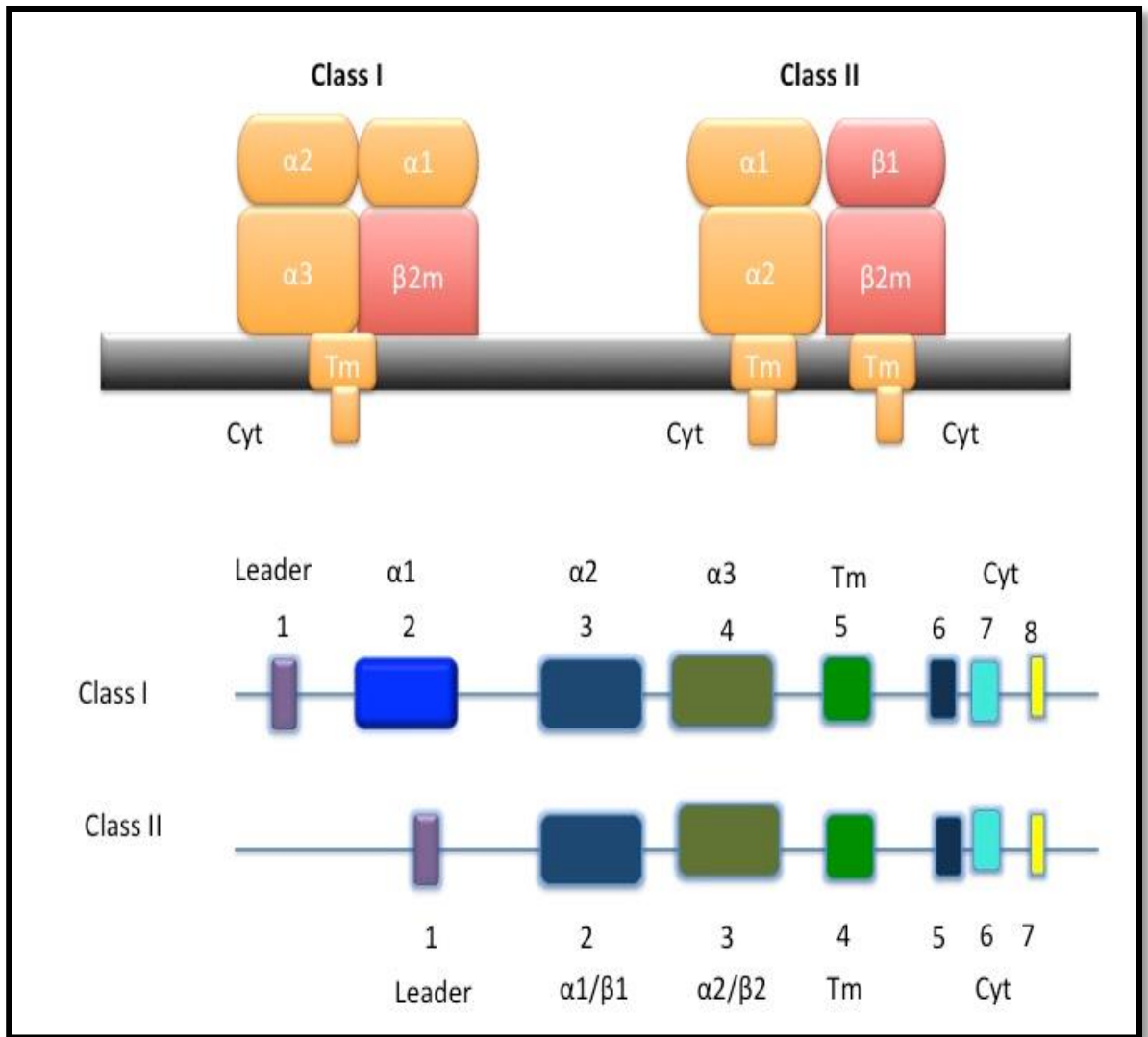


Figure 2 A schematic picture of MHC molecules and genes for class I and II; adapted from Rajalingam et al. (2010).

1.4.3 Fundamental Features of MHC: Polymorphism

The most important feature of MHC is extreme polymorphism. Polymorphism of MHC is characterised by extraordinarily large numbers of alleles and the nucleotide sequences between alleles can differ at multiple sites (Apanius et al. 1997). In HLA, Immuno Polymorphism Database (IPD) has provided the most update information on the number of alleles, with more than 2000 alleles having been reported at class I, and more than 1000 at the class II (Robinson et al. 2013). MHC is recorded as the most polymorphic gene in the mammalian genome (Erlich, 2012), with exception of several wild animals such as moose and bison (Mikko et al. 1999). This might may be a consequence of genetic bottleneck (Ujvari & Belov 2011).

MHC polymorphism is associated with diversity of antigen presentation and there is a believe that MHC polymorphism predates speciation and the polymorphisms are long-lived (Figuerola et al. 1988). This mechanism is called trans-species polymorphism (Klein 1987). It is characterised by retention of alleles across species leading to discordance between species trees and alleles phylogenetically (Figuerola et al. 1988). However, it has been argued that the polymorphism of the HLA allele are of more recent origin (Bergstrom et al. 1998).

MHC diversity has been thought to be due to recombination processes, resulting in exchange of segments between alleles or loci. Recombination includes gene conversion and crossing over (Adamek et al. 2015). Gene conversion is defined as transfer of genetic material from a donor to an acceptor gene without the donor being changed in the process (one chromosome to its homolog), while, crossing over involves bidirectional transfer of genetic material between homologous chromosomes. In 1991, Gyllensten & colleagues suggested that allelic diversity of DRB1 may have originated from different variant mixtures of two structural domains in primates. Recently, a study by Adamek et al. (2015) that used seven novel HLA alleles has supported the involvement with gene conversion in shaping diversity of MHC. In addition, the study also highlighted intralocus and interlocus gene conversion among HLA alleles. While, in a study of MHC diversity in a sheep, Schwaiger et al. (1993) advocate that the DRB polymorphism may be generated by double-recombination or/and gene-conversion-like events. Studies in other animals such as American bison and cattle also support the

importance of recombination process in shaping MHC diversity (Ohta, 1995; Mikko et al. 1997).

MHC polymorphisms are believed to be maintained by pathogen-driven balancing selection. There are three types of pathogen-driven balancing selection; heterozygote advantage, negative frequency dependent selection and fluctuating selection (reviewed by Meyer & Thomson, 2001; Stefan et al. 2014). Heterozygote advantage is believed that cause of maintenance of MHC class II gene polymorphism in sheep (Stear et al. 2005). The divergent allele advantage is one of the heterozygote advantage form (Wakeland et al. 1990) and with divergent allele advantage as a selection mechanism in a model, several key features of MHC were well explained, thus supporting the idea of MHC polymorphisms are maintained by heterozygote advantage (Stefan et al. 2014).

1.4.4 MHC Linkage Disequilibrium

In humans and animals, there is growing interest in the diversity of the MHC in the genome. One interesting pattern of diversity in the MHC is linkage disequilibrium. Linkage disequilibrium is the non-random association between alleles at different loci (Ardlie et al. 2002). Linkage disequilibrium is observed when a particular allele at one locus is inherited together on the same chromosome with a particular allele at a second locus more regularly than expected (Ardlie et al. 2002). The level of linkage disequilibrium between markers is influenced by molecular and genetic factors (Kauppi, 2003).

Different measures are available for linkage disequilibrium and have been reviewed extensively (Slatkin, 2008). The first measurement of linkage disequilibrium was introduced by Lewontin (1964) who used coefficient of linkage disequilibrium (D) but had several weaknesses. The square of the correlation coefficient (r^2) is an alternative which can be more robust and less prone to overestimate linkage disequilibrium (Ardlie et al. 2002; Lee et al. 2012). Recently, asymmetric linkage disequilibrium (ALD) measures have been developed by Thomson & Single (2014) which tend to be more appropriate and informative especially when there is an uneven number of alleles at each locus.

High linkage disequilibrium is recorded in the MHC in humans as well as in animals. A previous study in 39 human families has revealed high LD across the DRB1, DQA1 and DQB1 regions (Begovich et al. 1992). In addition to that, they also detected a strong linkage disequilibrium between the haplotype DRB1-DQA1-DQB1 and HLA-B. Interestingly, Klitz et al. (1995) found a strong linkage disequilibrium present between DR-DQ and DPB1. In the cattle, Andersson & Rask (1986) provided the evidence of strong linkage disequilibrium between DR-DQ genes. It was also evident that the linkage disequilibrium occurred between the class I lymphocyte antigen G13br and the allele G2 in sheep (Stear et al. 1996).

1.5 Sheep MHC or Ovar-Mhc

The ovine MHC or Ovar-MHC ('Ovar' representing *Ovis aries*) was discovered from serological studies on sheep lymphocyte antigen. The Ovar-MHC previously known as ovine Lymphocyte Antigen (OLA) is located on the long arm of ovine chromosome 20 (OAR 20q15-20q23) (Hediger et al. 1991). This organization distinguishes the Ovar-MHC from the MHC of humans and rodents, which are located on chromosome 6 and chromosome 17 respectively (Kelly et al. 2005).

Studies of the Ovar-MHC over several decades have revealed a reasonable picture of the genetic organisation and function of the genes. Like MHC in other mammals, Ovar-MHC is mainly partitioned into three distinct regions, classes I, II and III with the class I region telomeric to the class II and class III regions (**Figure 3**). The physical mapping of Ovar-MHC region was accomplished by means of a 190,000 BAC clone by Liu et al. (2006). Later, a complete sequence of the Ovar-Mhc classes I, II and III was published by Gao et al. (2010) using DNA shotgun sequencing of overlapping 26 BAC clones. They have identified 177 protein-coding genes on the basis of open reading frames (ORF) with approximately 2,434, 000 nucleotides in length within Ovar-MHC. The complete MHC sequence obtained from this work and a comparison sequence analyses with human and cattle sequences revealed a high conservation in the MHC structure and loci order except for the class II.

The class I–class III contig spans approximately 1.9 Mb on chromosome 20 (Dukkipati et al. 2006b). The Ovar-MHC class I contains 1.3 Mb and the Ovar-MHC class III region is 600 kb (Liu et al. 2006). The class IIa and class IIb contigs span approximately 400

and 300 kb respectively (Liu et al. 2006). The Ovar-MHC class I contains classical class I genes and other non-classical MHC genes (Miltiadou et al. 2005). The Ovar-MHC class II cluster comprises the classical class IIa genes (Ovar-DQ and -DR) and the class IIb genes (DNA, DOB, DYA, DYB, DMA and DMB) (Dukkipati et al. 2006b). While, the Ovar-MHC class III contains a high density of genes includes several genes which have been identified as important in innate immunity, for example genes coding for C4 and TNF (Dukkipati et al. 2006b).

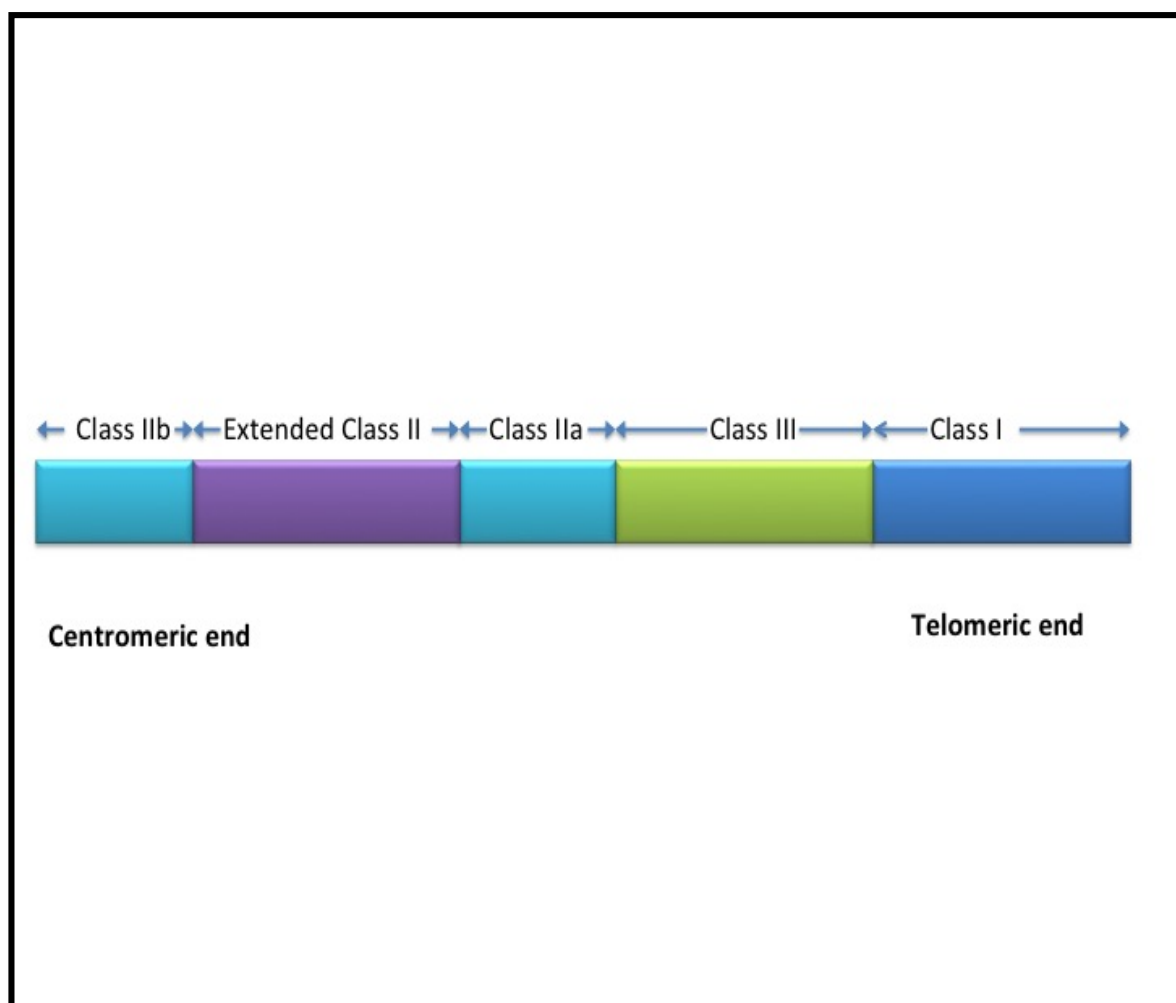


Figure 3 A schematic picture of Ovar-MHC on chromosome 20. The Ovar-MHC class II is divided into class IIa and IIb by autosome insertion. This figure is adopted from Gao et al. (2010).

1.5.2 Ovar-Mhc Class II Region

The Ovar-MHC class II region is the area of special interest in this study. The class II region is the best-characterized region and associated with the development of the

specific immune response to parasites (Dukkipati et al. 2006b). A distinct feature of the sheep class II compared with other species is that class II splits into two clusters (**Figure 3**). These two clusters are called class IIa and class IIb, which are separated by an inversion. This division is similar to an observation in bovine MHC (BoLA) (Childers et al. 2006). Recently, the inversion region complete sequence has become available through the work of Li et al. (2012) using a BAC clone. They have revealed that the arrangement and genetic architecture of this inversion/insertion is similar to cattle. Thus, their work gives further support to the previous hypothesis that ancient chromosome rearrangement occurs through chromosome looping and later crossover in the ancestor ruminant (Amills et al. 1998).

1.5.3 Ovar-MHC class IIa: DR and DQ loci

The schematic structure of the Ovar-MHC Class IIa region is illustrated in **Figure 4**. Unlike HLA, the Ovar-MHC class IIa consists of DR and DQ loci without DP loci (Chardon et al. 1985). A detailed account of the genomic organization of MHC class IIa was published by Herrmann-Hoesing et al. (2008a) who used genomic DNA from Rambouillet sheep. The DQA1 neighbouring DRB1 and two DQ loci each comprise one DQA and one DQB gene positioned in tail-to-tail orientation. The DQA1 neighbouring with DRB1 was also observed from a BAC library using genomic DNA from Merino sheep (Liu et al. 2006). The transcription direction is the same for DQA1 and DQA2, while DRB1, DQB1 and DQB2 loci are transcribed in the opposite way (Herrmann-Hoesing et al. 2008a). A previous report using 20 novel SNPs of class II provides the evidence that some region of class IIa in sheep is a 'SNP desert' which characterized with low heterozygosity (Lee et al. 2012). The class IIa, IIb and III subregions are together creating the haplotypic block which showed low frequency of recombination within these three sub regions (Lee et al. 2012).

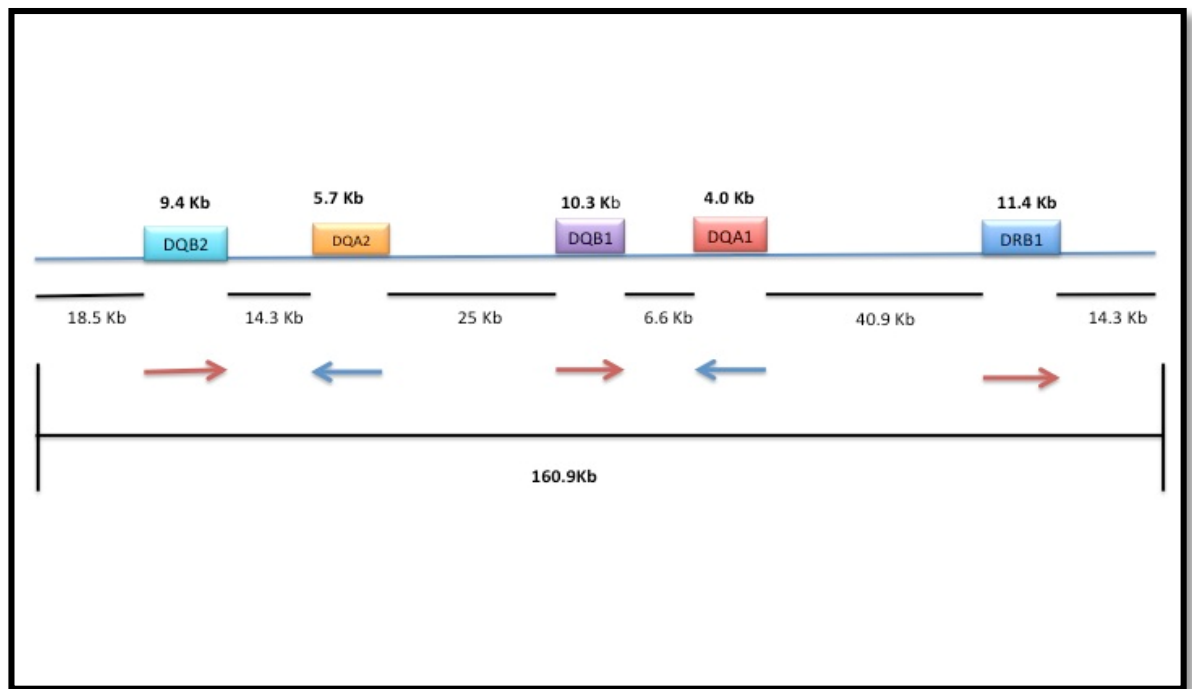


Figure 4 Schematic picture of Ovar-Mhc class IIa loci in a Rambouillet ram; modified from Hermann-Hoesing et al. (2008a). The red and blue arrows indicate of transcription process.

1.6 Ovar-DR Genes

DR molecules are made up of α and β chains. The DRA gene encodes the α chain of the DR molecule. On the other hand, the DRB gene encodes the β chain of the same molecule.

1.6.1 Ovar-DRA

The existence of a single DRA gene has been demonstrated in a Southern hybridization study (Scott et al. 1987). The Ovar-DRA has been shown to have a low number of polymorphisms by RFLP (Fabb et al. 1993; Escayg et al. 1996). Low polymorphism or monomorphic DRA gene has also been reported in cattle (Gowane et al. 2013).

1.6.2 Highly Polymorphic of Ovar-DRB1

In contrast to DRA, the genes that encode the β chain of the DR molecule or DRB gene are highly polymorphic. There are four DRB loci in sheep (Dukkipati et al. 2006b). However, only one of the four is a functional gene namely DRB1, and the remaining three are pseudogenes, DRB2, DRB3 and DRB4. The pseudogenes lack exon 1 and 2

(Dukkipati et al. 2006b). The polymorphisms of the DRB1 exon 2 have been focussed on in many studies as this region is important in encoding glycoprotein dimmers (Fremont et al. 1996).

DRB1 is believed to be analogous to the first domain (β 1) in HLA-DR1 (Brown et al. 1993). Among Ovar-MHC class II genes, the expressed DRB1 locus was the most polymorphic with more than 100 distinctive DRB1 alleles having been reported in Genbank (Ballingall et al. 2011). Based on the sequencing-based typing, 38 Ovar-DRB1 exon 2 nucleotide sequences were recognised in a single study in sheep (Ballingall & Tassi 2010). Ovar-DRB1 contains six exons totalling 801 bp (Hermann-Hoesing et al. 2008a).

1.6.3 Database IPD-MHC and Standard Nomenclature of DRB1 locus

The MHC sequences of multiple species have been reported in the Immuno Polymorphism Database-MHC (IPD-MHC) website. The IPD-MHC website sequence submission tools provide continuous updating of new allele sequences. It offers the opportunity for investigators to submit new allele/alleles by submitting a novel complete sequence. The minimum requirement for submission to this database is a complete sequence of the second exon. For sheep, the IPD-MHC-OLA is the platform that provides the updated information on allelic diversity (<http://www.ebi.ac.uk/ipd/mhc/ovar/index.html>). There are more than 100 Ovar-DRB1 sequences submitted in the website (Ballingall & Tassi, 2010).

The allelic group assignments were based on regions that encode for the peptide-binding domains. The region includes polymorphisms in the exon 2 and 3 sequences for class I alleles, and exon 2 sequence for class II alleles (Rajalingam et al. 2010). The Ovar-DRB1 allelic assignments are designated in accordance with the MHC nomenclature system. According to the MHC nomenclature, the Ovar class II alleles are designated by the prefix Ovar and their gene locus (e.g. Ovar-DR, Ovar-DQ), followed by the letter "A" or "B" to represent the polymorphic α and β chains of the Ovar-DR, Ovar-DQ (e.g. Ovar-DQA, Ovar-DRB) and only by the letter "B" for Ovar-DR, as this is its only polymorphic chain (e.g. Ovar-DRB). As some regions have various genes, each locus is given number (e.g. Ovar-DRB1). The first two digits assigned after the species and locus designation represents the allelic family (e.g. Ovar-DRB1*01). The same

family alleles do not differ by more than four amino acids from the second exon. This is followed by the other set of digits representing coding change within the same family allele (e.g. Ovar-DRB1*0101). The next set of digits represents synonymous or silent substitution in a coding region (e.g. Ovar-DRB1*010102) (Ballingall et al. 2011).

1.6.4 Multiple Techniques to Dissect Ovar-DRB1 Polymorphisms

Multiple techniques have been used to dissect polymorphisms of the DRB1 locus, and different numbers of alleles amplified in different breeds (**Table 3**). RFLP was initially used to dissect polymorphisms of DRB1 using a DRB1 exon 2 specific probe (Blattman et al. 1993). However, this methodology is frequently problematic because of extensive cross hybridization between the DRB probe and the DQB locus (Escayg et al. 1996). In addition, high cost is involved in use of restriction enzymes with large numbers of samples, and the technique is not able to discriminate between a large number of alleles (Buitkamp & Epplen 1996).

Single strand conformation polymorphism (SSCP), a technique which is based on the electrophoretic mobility of a single strand of DNA, also been described for typing of the DRB1 locus (Jugo & Vicario 2000). This technique is effective to capture polymorphisms and facilitate low cost genotyping (Gasser et al. 2006). However, SSCP suffers from technical problems such as high rate of reannealing of DNA strands and appearance of multiple bands from a double-stranded PCR product (Schwieger & Tebbe, 1998).

An RNA-based approach has also been used to capture DRB1 polymorphisms. Reverse transcription-PCR (RT-PCR) using the primers located on conserved regions of exons 1 and 3 has enabled the identification of the diversity of DRB1 together with a functional of gene from cDNA fragments (Herrmann et al. 2005; Herrmann-Hoesing et al. 2008a).

Another common technique is called sequence-based typing or direct sequencing. It is a simple method used to detect all MHC polymorphisms (Sayers et al. 2005b; Ballingall & Tassi, 2010). Sequence-based typing involves typing of specific coding regions of MHC genes, with direct sequencing of the PCR amplicons. However, the challenge posed by this technique is the need to design the primers that is able to detect all polymorphism (Ballingall & Tassi; Rajalingam et al. 2010).

Microsatellite or simple tandem repeat (STR) have been used to assess the diversity of Ovar-DRB1 (Schwaiger & Epplen 1995; Schwaiger et al. 1995). For example, Ovar-DRB1 possesses a STR [(GT) n (GA) m] which exists in intron 2 (Schwaiger & Epplen 1995) and sequencing of this STR together with exon 2 was able to capture polymorphisms of DRB1 (Schwaiger et al. 1995). Schwaiger et al. (1995) have shown a high correlation between PCR products and alleles. However, this technique fails to differentiate some of the alleles (Stear et al 2005).

Different numbers of Ovar-DRB1 alleles amplified with different techniques are summarised in **Table 3**. One of the interesting observations from previous studies is that the number of alleles amplified in similar breeds is different. This could be explained due to different number of samples or technique used. The difference may also be attributable in part to the different allele profile in different breeds.

Table 3 Different numbers of alleles of the Ovar-DRB1 gene in multiple breeds of sheep. Adapted from Dukkupati et al. 2006a

Breed	Typing Method	No of sheep	No of alleles	Reference
Single Breed				
Arabi	1	111	8	Lotfi et al. 2012
Blue Du Maine	2	1	2	Ballingall & Tassi (2010)
Bluefaced Leicester	2	2	3	Ballingall & Tassi (2010)
British Milk/ Suffolk cross	2	20	13	Ballingall & Tassi (2010)
British Milk/ Texel cross	2	16	13	Ballingall & Tassi (2010)
Cheviot	2	3	6	Ballingall & Tassi (2010)
	2	20	14	Konnai et al. 2003b
Chinese Merino	1	204	16 genotypes	Shen et al.2014
Columbia	3	9	6	Hermann-Hoesing et al. 2005
	3	129	17	Hermann-Hoesing et al. 2008b
Corriedale	2	6	9	Konnai et al. 2003b
Greyface	2	9	11	Ballingall & Tassi (2010)
Karakul Ram	2	33	24	Polat et al. 2014
	2	156	40	Larruskain et al. 2010
Karrantzar	4	17	4	Jugo & Vicario (2000)
Laxta	4	83	8	Jugo & Vicario (2000)
Lleyn	2	1	2	Ballingall & Tassi (2010)
Merino	5	130	8	Outteridge et al. 1996
	5	234	16	Bot et al. 2004
	6	189	29 bands	Blattman et al. 1993
North Ronaldsey	2	1	2	Ballingall & Tassi(2010)
Polish Heath	1	101	65 haplotypes	Gruszczynska et al. 2005
Polish Lowland	1	99	68 haplotypes	Gruszczynska et al. 2005
Prealpe	6	89	10*	Grain et al. 1993
	2	2	4	Ballingall & Tassi(2010)
Polypay	3	8	5	Hermann-Hoesing et al. 2005
	3	126	21	Hermann-Hoesing et al. 2008b
Rambouillet	3	15	10	Hermann-Hoesing et al. 2005
	3	128	26	Hermann-Hoesing et al. 2008b

Breed	Typing Method	No of sheep	No of alleles	Reference
Scottish Blackface	7	21	8	McCrie et al. 1997
	7	299	17	Buitkamp & Epplen (1996)
	7	179	19	Schwaiger et al. 1995; Stear et al. 1996
	2	64	18	Ballingall & Tassi (2010)
Scottish Blackface cross	2	77	20	Ballingall & Tassi (2010)
Scottish Mule	2	2	3	Ballingall & Tassi (2010)
Soay	2	15	5	Paterson (1998)
	5	1209	8	Paterson et al. 1998
Suffolk	2	71	28	Konnai et al. 2003b
	2	179	7	Sayers et al. 2005b
	2	5	5	Ballingall & Tassi (2010)
	1	52	13 haplotypes	Konnai et al. 2003b
Suffolk/Texel cross	2	9	7	Ballingall & Tassi (2010)
Texel	2	155	8	Sayers et al. 2005b
Texel/unknown cross	2	2	3	Ballingall & Tassi (2010)
Mixed Breed				
Four different breeds	2	15	13	Schwaiger et al.1993
Coopworth, Landrace, Merino, Perendale, Romney and Texel	2	34	34	Schwaiger et al. 1994
Finsheep and Russian Ramanov	4	31	9	Kostia et al. 1998
Lori-Bakhtiari, Shaul and Zandi	1,2	92, 40,47	14 haplotypes	Nikbakht et al. 2011
Xinjiang Karakul Ram Bashibai populations and Bashibai/AltaiArgali	2	116	42	Polat et al.2014

1= PCR-RFLP of exon 2

2= PCR amplification and sequencing of exon 2 either alone or together with a part of adjacent intron

3= RT-PCR of exon 1and 3 from cDNA

4= SSCP and sequence analysis of exon 2

5= Length polymorphism of microsatellite in intron 2

6= RFLP with exon 2 specific probe

7= Length polymorphism of STRs in intron 2 plus hybridization of oligonucleotides within exon 2

* Existence of more than one locus has been determined

The frequency distribution of Ovar-DRB1 alleles is of particular interest in Ovar-MHC research. The information aids in the understanding of the lineage of breed (Hermann-Hoesing et al. 2005). Specifically, the Ovar-DRB1*1202, *0203, *0404, *0801 and *1101 are possibly common alleles from Spanish and English descent sheep (Hermann-Hoesing et al. 2005). The most frequent alleles in different breeds are reported in **Table 4**. From the table, it seems that DRB1*0702 has been reported frequently as the most common allele in previous studies.

Table 4 Association of breeds and their common alleles reported in multiple studies

Origin	Common allele	Frequency	Reference
Asia			
Bashibai	DRB1*2F10c8 and DRB1*0803	13.2	Polat et al. 2014
Bashibai/ Altai Argali cross:			
-F1	DRB1*2F16c2	17.6	Polat et al. 2014
-F2	DRB1*1601	14.3	
-F3	DRB1*0803	20.0	
Karakul Ram	DRB1*K18cC	21.2	
New Zealand			
Corriedale	DRB1*0201	25.0	Konnai et al. 2003b
Europe			
Cheviot	DRB1*0203	27.5	Konnai et al. 2003b
	DRB1*02032	8.7	Hermann-Hoesing et al. 2008a
Rambouillet	DRB1*1202	4.3	Hermann-Hoesing et al. 2008a
Scottish Blackface	DRB1*0101	35.0	Schwaiger et al. 1995; Stear et al. 1996
Suffolk	DRB1*0702	23.9	Konnai et al. 2003b
	DRB1*03411	NA	Sayers et al. 2005b
Texel	DRB1*0203	NA	Sayers et al. 2005b
South America			
Karrantzar	DRB1*0702	28.0	Jugo & Vicario (2000)
Laxta	DRB1*0702	32.0	Jugo & Vicario (2000)
	DRB1*0702	11.5	Larruskain et al. 2010

1.6.5 Ovar-DRB1 Association Studies

Studies on the association of Ovar-DRB1 with resistance to important veterinary diseases have also been undertaken (**Table 5**). In Scottish Blackface lambs, Ovar-DRB1 G2 allele was found to be significantly associated with *T. circumcincta* infection (Schwaiger et al. 1995; Stear et al. 1996). In addition, the substitution of the prevalent allele I, with the allele G2 was found to be significantly associated with dramatic decreases of FEC (Stear et al. 2005). Further investigation in Suffolk sheep also suggested an association with the same allele and resistance to GIN (Sayers et al. 2005). Interestingly the other two alleles (OAMHC213 and Ovar-DRB10) also influenced susceptibility to GIN. In the free-living Soay population examined by Paterson et al. (1998), the OLADRB257 allele is associated with strong resistance.

Ovar-DRB1 allele was also associated with resistance against specific viral diseases (**Table 5**). In Chinese Merino sheep, Shen et al. (2014) have investigated the relationship between DRB1/DQB1 gene polymorphism and cystic echinococcosis. They found that the DRB1-Saclab/DRB1-Mvalbb/DQB1-Taqlaa/DQB1-HaeIIInn haplotype is echinococcosis resistant. The other study involved three breeds; Columbia, Polypay and Rambouillet has shown that the specific expression of Ovar-DRB1*0403 and DRB*07012 alleles was associated with low levels of the virus of OPPV (Herrmann-Hoesing et al. 2008a). While, another researchers have demonstrated that the DRB1*0325 allele was associated with susceptibility with the same virus (Larruskain et al. 2010). In addition, they have also identified the Ovar-DRB1*0702 as a resistant allele against ovine pulmonary adenocarcinoma (OPA), and alleles such DRB1*0143 and DRB1*0323 are considered as a susceptible allele against OPA (Larruskain et al. 2010; 2012).

Table 5 Association of Ovar-DRB1 with disease resistance reported in previous studies

Disease	Breed	Allele	Type of association	Reference
Parasite				
Nematode	SBF	DRB1*0203	Resistance	Schwaiger et al. 1995; Stear et al. 2005
	Soay	OLADRB257	Susceptible	Paterson et al. 1998
	Suffolk	OAMHC213 and DRB10	Susceptible	Sayers et al. 2005b
	Suffolk	DRB1*0203	Resistance	Sayers et al. 2005b
Cystic Echinococcosis	Chinese Merino	SRB1-SacIab/DRB1-Mvalbb/ DQB1-Taqlaa/DQB-HaeIIInn (haplotype)	Resistance	Shen et al. 2014
Virus				
Ovine progressive pneumonia virus (OPPV) or Maedi-Visna (Maedi)	Columbia, Polypay and Rambouillet	DRB1*0403 and DRB1*07012	Resistance (lower level of OPP)	Hermann-Hoesing et al. 2008a
	Laxta	DRB1*0325	Susceptible	Larruskain et al. 2010
Ovine Pulmonary Adenocarcinoma (OPA)	Laxta	DRB1*0702	Resistance	Larruskain et al. 2010; 2012
	Laxta	DRB1*0143, DRB1*0323	Susceptible	Larruskain et al. 2010

Specific amino acid residues of the Ovar-DRB1 allele play a pivotal role in determining the type and magnitude of the T-lymphocyte response to specific diseases (Hermann-Hoesing et al. 2008b; Larruskain et al. 2012). The studies have detailed the specific amino residues at the DRB1 locus association with several diseases is given in **Table 6**.

Table 6 Association of specific of amino acid positions with resistance or susceptibility against several diseases

Disease	Association with	Amino Acid Position	Reference
Ovine progressive pneumonia virus (OPPV) or Maedi-Visna (Maedi)	Susceptible	H32, A38, I67	Hermann-Hoesing et al. 2008a
	Resistance	Y31, T32, T51, Q60, N74	
Bovine Leukaemia Virus (BLV)	Resistance	R70 and K71	Nagaoka et al. 1999
	Susceptible	S70 and R71	Konnai et al. 2003c
Ovine Pulmonary Adenocarcinoma (OPA)	Resistance	Y31, T32, N37, T51, Q60, A74, S70, F86	Larruskain et al. 2012
	Susceptible	N42, T74, I86	

1.7 Ovar-DQ Genes

Ovar-DQ genes encode the DQ molecules. In cattle, DQ molecules are known to be equally important as DR molecules for the presentation of peptide antigens to T cells (Norimine & Brown 2005). As sheep and cattle are closely related, it is likely that DQ molecules are important for the same function and there have been many attempts to characterise DQ genes in sheep which will be discussed in the next section.

1.7.1 Ovar-DQ genes: Ovar-DQA and DQB

The presence of DQ genes in sheep was confirmed by the work of Chardon et al. (1985). They used genomic Southern blot analysis using probes which bind to the HLA DQ region. In a later study, two DQA genes per haplotype were observed in Ovar-MHC from

sequences of DNA clones and cDNA clones (Scott et al. 1991a; Fabb et al. 1993). This is consistent with a genomic organization of the DQ sub-region reported by Wright & Ballingall (1994). As mentioned earlier, there are two DQ loci each containing two DQA and two DQB genes, organized in tail-to-tail orientation (Hermann-Hoesing et al. 2008b). The two loci are 22-25 kb apart and are linked on a linear tract of 130 kb and 160 kb of DNA (Wright & Ballingall 1994; Hermann-Hoesing et al. 2008b). The DQA1 and DQA2 loci transcribed in the opposite direction from DQB2 and DQB1, and they contain four exons both totalling 768 bp (Hermann-Hoesing et al. 2008b).

1.7.2 Ovar-DQA: A Highly Polymorphic Gene

The DQ molecules that are encoded by DQ genes are vital for antigen presentation (Hickford et al. 2004). One interesting feature of Ovar-DQA1 is that 10-18% of sheep are reported to completely lack of the DQA1 gene or referred to as DQA1-N, suggesting that the number of DQA genes varies among haplotypes in an earlier investigation (Snibson et al. 1998). However, the duplication at the DQA2 locus or DQA2-like sequences was associated with DQA1 null. Thus, it maintains two DQA loci per haplotype in sheep (Hickford et al. 2000). Interestingly, these DQA2-like sequences are characterised to be more closely related with cattle DQA3 and DQA4 sequences compared with sheep DQA2 sequences (Hickford et al. 2004). There is evidence of historical recombination at DQA (Hickford et al. 2007). The diversity of both DQA1 and DQA2 alleles has been well characterized in previous works (**Table 7**). Generally, DQA2 seems to be more polymorphic than the DQA1. Common DQA2 alleles or haplotypes have been reported (**Table 8**). However, there were no specific patterns observed.

Table 7 Polymorphisms of the Ovar-DQA gene reported in multiple breeds of sheep

Breed	Typing Method	No of sheep	No of alleles	Reference
DQA1				
Romney, Coopworth/Perendale, Corriedale and others	RFLP	48, 19,222,50	8	Escayg et al. 1996
Merino, Romney	PCR-SSCP	NA	6	Snibson et al. 1998
Merino, Corriedale, Borderdale, Romney, Awassi and Finnish Landrace	PCR-SSCP	300	14	Zhou& Hickford (2004)
Merino, Corriedale, Romney and others (New Zealand crossbred sheep)	PCR-SSCP	520	12	Hickford et al. 2007
DQA2				
Romney, Coopworth/Perendale, Corriedale and others	RFLP	48, 19,222,50	16	Escayg et al. 1996
Merino, Romney	PCR-SSCP	NA	10	Snibson et al. 1998
6 breeds; Merino, Corriedale, Borderdale, Romney, Awassi, Finish Landrace	PCR-SSCP	2000	23	Hickford et al. 2004
Variety of breeds	PCR-SSCP	40,000	22	Hickford et al. 2007
3 breeds: German Mutton Merino, German Merino and German Blackheaded Mutton	PCR-SSCP	347,115, 175	21	Ennen et al. 2009
Chios	PCR-SSCP	400	20	Gelasakis et al. 2013

Table 8 Common DQA2 alleles or haplotypes found in different breeds of sheep

Breed	Common allele/ haplotypes	Frequency (%)	Reference
Merino, Corriedale, Borderdale, Romney, Awassi, Finish Landrace	DQA2*0101- *1401	13.2	Hickford et al. 2004
Variety of breeds	DQA2*1201 and DQA2*0101- *1401	15.8 and 14.5	Hickford et al. 2007
German Mutton Merino, German Merino and German Blackheaded Mutton	DQA2*0103 and DQA2*0601	25.9 and 15.9	Ennen et al. 2009
Chios	DQA2*0301	31.7	Gelasakis et al.2013

Bold indicate the Ovar-DQA2-like sequences

1.7.3 Nomenclature of DQA genes

Ovar-DQA1 and DQA2 gene nomenclature is based on those for bovine leukocyte antigen (BoLA) (Zhou & Hickford, 2004). Similarly, in Ovar-DRB1, the sequence is based on clones derived from PCR amplification; there must be at least three identical clone sequences. Names are constructed from the predicted amino acid sequences and comprised of four or five digits. The first two digits denote the major type, the third and fourth digits specify the subtype, whereas the fifth digit indicates silent substitutions. Alleles that differ by less than five amino acids in the first domain are considered as subtypes within a single major type. However, unlike Ovar-DRB1, the Ovar-DQA alleles have been not updated in the IPD-MHC-OLA.

1.7.4 Ovar-DQA Alleles and Haplotypes

Strong linkage disequilibrium shown in the MHC loci allows researchers to report findings in terms of haplotypes rather than by individual alleles (Rajalingam et al. 2010). In addition, the haplotypes have been shown to be a good tool for identifying complex diseases (Clark, 2004). First, the statistical power of association tests with haplotype data is expected to be enhanced due to reduction in dimension. Second, the protein of the candidate genes occur in polypeptide chains whose physical properties may depend on specific amino acids combination. Third, genetic variation in populations is inherited as a haplotypes (Clark, 2004).

The MHC OLA Nomenclature Committee has not yet established a nomenclature system for Ovar-MHC class I and II haplotypes. However, DQA haplotypes in sheep have been reported by Hickford et al. (2007) (**Table 9**).

Table 9 Haplotypes found in two DQA genes. Adapted from Hickford et al. 2007

Breed	DQA1	DQA2	DQA2 like
41 sires in New Zealand	0104	1201	-
	0402	0101	-
	0601	1101	-
	0101	0602	-
	0101	0103	-
	0103	0602	-
	0301	1201	-
	0401	08011	-
	0701	0901	-
	0302	1201	-
	0901	0901	-
	0301	0901	-
	0501	0601	-
	0103	1101	-
	0601	0602	-
	0501	1101	-
	0901	0601	-
	0103	0601	-
	0801	1001	-
	0104	0301	-
	0901	0301	-
	Null	Null	-
Merino, Corriedale,	-	0101	1401
Romney and Others New	-	0102	1601
Zealand crossbred sheep	-	0401	1501
	-	0102	1401
	-	0402	1701
	-	0702	1401
	-	0701	1401
	-	0401	1401
	-	0101	1601
	-	0701	1301
	-	0401	1601
Merino and Others New	-	0702	1601
Zealand crossbred sheep	-	0701	1601

1.7.5 Association of Ovar-DQA and Diseases

In humans, the polymorphism of DQA has been linked with the development of several autoimmune diseases such as insulin-dependent diabetes mellitus (Glass & Giannini, 1999). In sheep, it has been reported that lack of Ovar-DQA1 is linked with susceptibility to GIN (**Table 10**). A microarray-based expression study has shown that in a susceptible selection line, more expression of Ovar-DQA1 null alleles was observed (Keane et al. 2007). The susceptibility was associated with the hypothesis of failure in presenting parasite peptides to T cells. However, this association was found in only one (Perendale) of three sheep breeds examined (Keane et al. 2007). This suggests that increased expression of Ovar-DQA1 null alleles or a lack of DQA1 alleles is not a cause of susceptibility itself (Keane et al. 2007). Other multiplier factors such as a mixture of susceptible alleles, linkage disequilibrium between non-MHC with Ovar-DQA1 and expression levels of Ovar-DQA1 on APCs or a mixture of these factors are possible influence (Keane et al. 2007). Forrest et al. (2010) has investigated further the role Ovar-DQA1 null allele in nematode resistant in four different breeds (NZ Merino, South Africa Meat Merino, Polwarth and Corriedale), however no universal association was found between the allele and FEC. They only found a significant association with the presence of Ovar-DQA1 null with low GIN in only one breed.

On the other hand, the presence of specific Ovar-DQA2 allele was associated with higher susceptibility against ovine foot rot (see **Table 10**). Escayg et al. (1997) suggested that the presence of Ovar-DQA2*1101 increased the risk of susceptibility to foot rot infection. Later, Ennen et al. (2009) showed that the likelihood of a foot rot infection is less for ewes having one of the DQA2–DQA2-like haplotypes 0101–1401 (G) and 0702–1401 (J2) than for ewes carrying the alleles Ovar-DQA2*1101(E). The study by Gelasakis et al. (2013) provides further evidence that Ovar-DQA2*1101 is associated with higher susceptibility to foot rot.

Table 10 List of associations of Ovar-DQA alleles with important diseases in sheep

Disease	Allele	Breed Examined	Type of association	Reference
Nematodes	DQA1*N	Perendale, Romney and Coopworth	Susceptible (only in Perendale)	Keane et al. 2007
		NZ Merino, South Africa Meat Merino, Polwarth and Corriedale	Susceptible (only in South Africa Meat Merino)	Forrest et al. 2010
	DQA2*1101	Corriedale	Higher susceptibility	Escayg et al. 1997
Ovine foot rot	DQA2*0101/ DQA2*1401 or DQA2*0702/ DQA2*1401	German Mutton Merino, German Merino and German Blackheaded Mutton	Resistance compared with DQA2*1101/ DQA2*0501	Ennen et al. 2009
	DQA2*1101	Chios	Higher susceptibility	Gelasakis et al. 2013

Bold type indicates the DQA2-like sequence, the duplicated allele

1.7.5 Ovar-DQB and Polymorphisms

There is an indication that MHC class II loci are homologous with HLA-DQB in sheep (Deverson et al. 1991). Ovar-DQB region is a highly polymorphic gene (van Oorschot et al. 1994) with two DQB genes in sheep, namely DQB1 and DQB2 (Hermann-Hoesing et al. 2008b). The nucleotide sequences of Ovar-DQB1 and Ovar-DQB2 are similar with >90% similarity reported (Wright & Ballingall, 1994).

Unlike DRB1, Ovar-DQB genes are less well characterized. Two typing systems have been developed for Ovar-DQB genes (**Table 11**). These include RFLP and reference-strand-mediated conformation analysis (RSCA). The results obtained from RSCA so far are most promising, with the finding of 16 new Ovar-DQB sequence (Feichtlbauer-Huber et al. 2000). In spite of these promising results, currently there is also a lack of information of DQB genes in sheep.

Table 11 Polymorphisms of the expressed Ovar-DQB gene in multiple breeds of sheep

Breed	Typing Method	No of sheep	No of alleles	Reference
Prealpe	PCR-RFLP	89	9	Grain et al. 1993
Romney, Coopworth/Perendale, Corriedale, Others	PCR-RFLP	48, 19,222,50	6	Escayg et al. 1996
Scottish Blackface	RSCA	10	16	Feichtlbauer-Huber et al. 2000

1.8 Thesis Objective

The importance of the MHC molecules in the regulation of the immune response, together with the numerous associations of MHC alleles with nematode resistance, have shed light on the use of MHC as a genetic marker for nematode resistance. Thus, the main aim of this study is to establish the role of MHC genes and nematode resistance in Texel population. If a significant association between nematode resistance and MHC was found, this may have benefits in the selective breeding of sheep with nematode resistance. In addition, this study also will help in establishing molecular typing methods for characterizing MHC class IIa genes.

This study has five specific objectives:

1. To establish a sequence-based typing system for MHC class IIa genes.
2. To characterize the Ovar-MHC class IIa diversity profile in Texel population.
3. To establish the haplotypes and extent of linkage disequilibrium in Texel population.
4. To determine the association between MHC class IIa haplotypes and nematode resistance in Texel population.
5. To investigate the evolutionary history of MHC class IIa genes.

CHAPTER 2

GENERAL MATERIALS AND METHODS

2.1 Introduction

This chapter describes the general materials and methods used in this study. Exact details of the modifications of assays and changes are described in the relevant chapters.

2.2 Previous Work

This thesis project is a continuation of previous work, the aim of which is to acquire better understanding of the mechanism of nematode resistance to GIN in sheep. In this section, a brief description of previous work will be elaborated as some of the previous data has been incorporated in achieving the objective of this thesis. The animal sampling and parasitological tests (FEC) described in this thesis had been carried out previously prior the author commencing the study (Bishop et al. 2004). Methods not performed by the author are acknowledged in the acknowledgment section and the succeeding works elaborated in this thesis were carried out using previously stored biological samples.

Briefly, Texel sheep were used in this thesis. A total of 235 Texel lambs from Roslin Institute's Blythbank farm were involved in this study. The flock has a detailed pedigree record (**Appendix 1**) and producing approximately 70 lamb per year. All sires are purebred Texel originating from Texel Sire Reference, homebred and purchased rams. The lambs were sampled on three occasions, July, August and September (lambs were 5, 6 and 7 months olds) in 1998-2000.

2.2.1 Parasitological Data: FEC

FECs were previously determined from the Texel breed using a modified saturated salt flotation technique described by Bishop et al. (2004). Eggs were assigned to *Nematodirus* spp. or Strongyle. The following genera are considered under Strongyle spp: *Oesophagostomum*, *Chabertia*, *Bunostomum*, *Trichostrongylus*, *Cooperia*, *Ostertagia*, *Teladorsagia* and *Haemonchus* (Bishop et al. 2004).

2.2.2 Blood Sampling

Blood samples were collected at the same time together with faecal sampling. The blood samples were obtained by jugular venepuncture into evacuated glass tubes containing 20mM disodium EDTA (Becton Dickinson UK Ltd, Oxford) as anticoagulant. Plasma and buffy coat were obtained by centrifugation at 1000xg for 20 minutes and stored at -20°C before use.

2.2.3 Anti-L3 IgE Measurement

The serologic specific for anti-L3 IgE was analysed previously by Murphy et al. (2010) using indirect ELISA. The transformation used was $(\text{IgE} + 0.001)^{0.25}$ in order to normalise the IgE value.

2.3 MHC Class II Sequence-based Typing

Figure 5 shows a simplified overview of the methods implemented in this thesis. This process was applied to the characterization of Ovar-DRB1, DQA1, DQA2 (DQA2-like), DQB1 and DQB2. Some specific modifications shall be specified in the research chapters, where relevant. All the composition and preparation of methods for all solutions and media are explained in detail in **Appendix 2**.

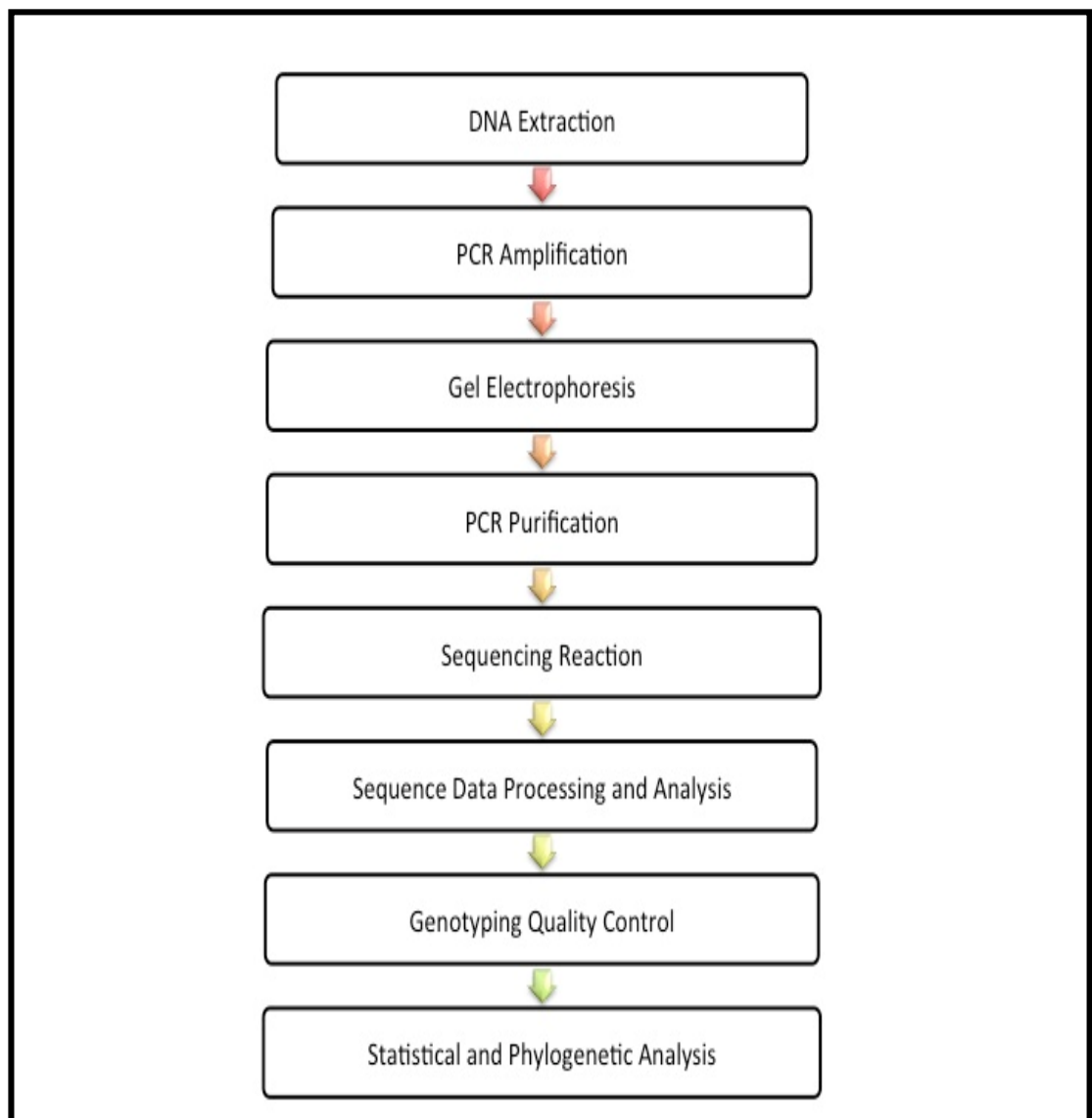


Figure 5 Main steps for sequencing-based typing in this study

2.3.1 DNA Extraction and Concentration Measurement

QIAamp DNA Blood Maxi Kits (Qiagen, Germany) were used to extract genomic DNA from the buffy coat, following manufacturer's recommendation. 500µl of QIAGEN proteinase K were mixed with a solution of 10ml thawed buffy coat (added phosphate buffered saline (PBS). 12ml of buffer AL was added and the solution mixed thoroughly. Next, the solution was incubated at 70°C for 10 min, followed by addition of 10ml of 100% of ethanol to the sample. This was mixed again through vigorous shaking. The solution was then transferred into a QIAamp Maxi Column and centrifuged at 1850g for 3 min.

Buffer AW1 (5ml) was added and the solution was centrifuged at 4500g for another 2 min. Later, buffer AW2 (5ml) was then added and was centrifuged at 4500g for 20 min. The column was placed in a centrifuge tube and the collection tube containing filtrate discarded. Buffer AE (1ml) was pipetted directly onto the membrane of the column, the cap closed and incubated at room temperature for 5 min and subsequently centrifuged at 4500g for 2 min. Buffer AE (1ml) was again pipetted directly onto the membrane of the column, followed by incubation at room temperature for 5 min, subsequently centrifuged at 4500g for 5 min.

DNA concentration was determined by pipetting 200 µl of mixture of each DNA sample and TBE buffer at a ratio 1:50, into a well of 96 well microtitre plate (Nunc, Denmark). A well containing 200 µl of water was used a reference standard. Results were obtained using a PowerWaveX Select Scanning Microplate Spectrophotometer and KC4 v3.0 with PowerReports™ data reduction software (BIO-TEK (Vermont, USA).The DNA samples were stored at -20°C until further used. Purity of DNA sample is indicated by the ratio of absorption values at 260nm and 280nm.

2.3.2 Polymerase Chain Reaction Amplification

Polymerase Chain Reaction (PCR) is a common laboratory technique to make copies of specific fragments of DNA. The specific PCR primers used to amplify the genomic DNA are listed in **Table 12**. The forward and reverse primers of Ovar-DRB1, DQA1, DQA2, DQB1 and DQB2 (100pmol/μl, Eurofins MWG Operon) were diluted with sterile water (Invitrogen, California, USA) to give a final concentration of 20 pmol/μl for each primer. The details of each primer design shall be discussed in the relevant research chapter.

PCR amplification was carried out in 96-well plates on a thermal cycler (Gene Amp- PCR system 2700 Version 2.0-Bio systems A&B) using 0.5 U Taq DNA polymerase (Qiagen), 0.5 μM of each primer, 25 mM of MgCl₂ (Qiagen), 150 μM dNTP (dNTPs Invitrogens, Germany) and genomic DNA in a reaction volume of 20 μL. All PCR reactions included a negative control. The PCR conditions were adjusted for each gene after optimization trials to reach the best melting temperature (the specific PCR conditions for each gene are described in research chapters and also in **Appendix 3**).

2.3.3 Agarose Gel Electrophoresis

Agarose gel electrophoresis was used for analysing DNA fragments. The gel sizes were made by melting agarose powder (Seakem® LE Agarose, Rockland, ME USA) in TBE buffer in a microwave oven. Gels were made routinely 1.5 % (w/vol). The gels were cast with the addition of ethidium bromide (50μg/ml) and using plastic combs for wells into which samples could be loaded. Once set, gels were submerged in TBE buffer in the electrophoresis tank. Samples were mixed with 5x loading dye (Qiagen) and loaded into the wells of the gel. Samples were subjected to electrophoresis for approximately 30min at 120 mV depending on the size and percentage of agarose of the gel. The DNA was visualized with a UV transilluminator.

Table 12 Primers used to amplify the second exon of the MHC class II gene

Amplification region	Primer Name	Primer Sequence
DRB1	ERB3	5'-CTC TCT CTG CAG CAC ATT TCC T-3'
	SRB3	5'-CGC TGC ACA GTG AAA CTC-3'
	DRB1_27F	5'-ATT AGC CTC TCC CCA GGA GTC-3'
	DRB1_27R	5'-CAC ACA CAC ACT GCT CCA CA-3'
DQA1	DQA1up	5'-ACC TGA CTC ACC TGA CCA CA -3'
	DQA1down	5'- AAC ACA TAC TGT TGG TAG CAG CA -3'
	NikDQA1 F	5'-ACT GGC CAC AAA TGA AGC CCA CAA-3'
	NikDQA1 R	5'-AGA AGG CAG AAG ATG AGG GTT CAG-3'
	DQA1_92.y085F	5'- CTC CGA CTC AGC TGA CCA -3'
	DQA1_92.y085R	5'-AAC ACT TAC TGT TGG TAG CAG CA -3'
	DQA1_Z28518 F	5'-CCC TGA CTC AGC TGA CCA CA-3'
	DQA1_Z28518 R	5'-AAC ACT TAC TGT TGG TAG CAG CA -3'
DQA2/ DQA2like	DQA2s-up	5'-ACT ACC AAT CTC ATG GTC CCT CT-3'
	DQA2s-down	5'- GGA GTA GAA TGG TGG ACA CTT ACC-3'
DQB1	JM05	5'-TCT CCC CGC AGA GGA TTT CGT G -3'
	JM06	5'-CTC GCC GCT GCC AGG TGA AGG- 3'
	991	5'-CTG ACC GAG CGG CTG T-3'
	994	5'-CGG CTC TCT GTC CCA TCC-3'
DQB2	JM05	5'-TCT CCC CGC AGA GGA TTT CGT G -3'
	JM07	5'-GCC GCT GCA AGG AGG TGA TGA G - 3'
	1005	5'-CTG ACC GAG CGG CTG TCT-3'
	1007	5'-CTC GCG CGC TGA GTC -3'
	MJS05	5'-TCC CCG CAG AGG ATT TCC TG -3'
	JM07	5'-GCC GCT GCA AGG AGG TGA TGA G - 3'

2.3.4 PCR Purification

The process of purification was undertaken using the QIAquick PCR Purification kit (Qiagen). Briefly, the genomic DNA adhered to the filter within the column, separating it from all other components of the PCR reaction, which were washed away with various buffer solutions. The genomic DNA was finally eluted with 30µl Elution buffer (EB). A gel was then prepared to determine banding strengths after purification. Samples with null and very weak bands were discarded at this stage.

2.3.5 Sequencing Reactions

Sequencing reaction master mix solution was prepared using primer, Sequencing Buffer (5X), sterile water and the Big Dye Terminator Cycle Sequencingv3.1 Ready Reaction Kit (ABI Prism) (**Table 13**). Two master mix solutions were made, one with the forward primer and one with the reverse primer. The concentration for each primer was 1pmol/µl. The forward and reverse master mix solutions were plated out into AB gene 96 well plates. PCR products were added to wells containing the forward and reverse mix. The plate was then carefully sealed using thermal film and placed in the PCR machine. The sequencing 'Big Dye' programme was run following the protocol in **Table 14**.

Table 13 The reagent of master mix solution for sequencing reaction

Reagent	Volume required (µl)
Sequencing primer	3.2
5x Sequencing Buffer	2
Big Dye	1
Water	1.8
PCR product	2

Table 14 The temperatures and times of 'Big Dye' program in the thermo cycler

Temperature (°C)	Time (min)
96	10
50	5
60	2
4	∞

2.4 Sequence Data Processing and Analysis

Sequences were read and evaluated manually by use of CLC Genomic Workbench v6.1 software (CLC bio, Denmark). Firstly, the sequences were trimmed and then followed with the assembling process of forward and reverse strand. The assembled sequence is called a consensus. The consensus was analysed and the polymorphisms in the sequence were then assigned a letter representing the appropriate substitution according to **Table 15**. This substitution is based on guidelines from the International Union of Biochemistry (IUB) ambiguity code (Nomenclature Committee of the International Union of Biochemistry (NC-IUB) 1984).

Table 15 Appropriate letters to be assigned to possible bases

Code	Base	Base	Base
R	A	G	-
W	A	T	-
M	A	C	-
Y	C	Y	-
S	C	G	-
K	T	G	-
D	A	G	T
H	A	C	T
B	C	G	T
V	A	C	G

Secondly, Basic Local Alignment Search Tool (BLAST) searches were performed against a local allele database. The local database is a collection of alleles, which have been identified through National Centre for Biotechnology Information (NCBI) and European Bioinformatics Institute (EBI) databases (**Appendix 4**). NCBI is a resource for genetics and contain publicly available databases (<http://www.ncbi.nlm.nih.gov/>) and it is especially important for retrieving information such as nucleotide or protein sequence. EBI is another particularly useful web resource for the same function (<http://www.ebi.ac.uk/>). The BLAST gave a list of percentage similarities of known alleles to the consensus sequence. By a process of elimination, it was then possible to

assign the alleles. The allele assignments were then made, relating these to existing sequences whenever possible. On occasions, where no complete match was obtained, it was suspected that a novel allele is present.

Table 16 illustrates example of the assignment of the alleles in five Texel lambs. The lambs have AJ238935 in the first column and asterisk in second column (98t009, 98t022 and 99t071). These animals were designated as homozygotes (only one DQB2 allele found). On the contrary, 98t023 and 99t008 lambs clearly are heterozygous at DQB2 locus, as two alleles were found in a single sample.

Table 16 A table shown the example of the DQB2 alleles found from five Texel lambs. The lambs found with one allele had an * in the second column.

Lamb	First Allele	Second Allele
98t009	AJ238935	*
98t022	AJ238935	*
99t071	AJ238935	*
98t023	AJ238935	AJ238937
99t008	AJ238935	AJ238933

2.5 Genotyping Quality Control

A crucial step in typing process for this study is quality control. Once the genotype was determined for each sheep, several steps for the quality control of the assignment were taken to task. This includes three essential steps namely cloning of suspected novel alleles, checking with haplotype and pedigree inheritance and re-examination of the null alleles.

2.5.1 Cloning of Suspected Novel Alleles

As mentioned earlier, in the typing process, novel alleles were discovered. These novel alleles were submitted to the European Bioinformatic Information (EBI) and the Immuno Polymorphism Database (IPD) database. However, suspected novel alleles sequence from heterozygous animals were checked by cloning. This cloning step is important for the validation and also to meet the requirement for inclusion in IPD-MHC database (Ballingall & Tassi, 2010; Ballingall et al. 2011).

The PCR products were TOPO® cloned into One Shot ® Mach1™ -TIR Competent Cells (chemically competent *E. coli* cells) were transformed with the recombinant vector according to the manufacturer's instruction. The reaction was mixed gently in a 0.5ml tubes (without vortexing) and incubated at room temperature for 20 min. The reaction was then placed on ice. The cloning reaction (2µl) was added to a vial of One shot *E. coli* mixed gently and incubated on ice for 30 min. The cells were heat-shocked for 30s at 42°C in a water bath, then removed and transferred directly into ice. RT SOC (250µl) was added and shaken horizontally at 37°C for 1hr. Cells (40µl) were then spread onto a pre-warmed agar plate and incubated at 37°C overnight. White colonies were picked and grown in 5ml LB broth containing 50 ug/ml ampicillin. Plasmid DNA was purified following the QIAprep spin miniprep kit protocol (Qiagen). At least three clones representing each allele were sequenced in both directions for verification.

2.5.2 Checking with Haplotype and Pedigree Inheritance

The individual haplotype for sire, dam and lambs was deduced, followed with checking of pedigree inheritance. The histocompatibility genes are well known to be co-dominantly expressed in an individual, one from each parent, and inherited as a haplotype (set of alleles) (Erlich 2012). By this concept, firstly we sorted the lambs by the same sire and dam by using the programme in the SAS (SORT BY). By using this means, all lambs from the same sire should possess similar haplotypes (except technical errors or recombination occurs) that they got from their sire and dam. Occasionally, we identified some of the lamb haplotypes which differed from its parent. We then, re-examined the particular gene sequence or repeated genotyping to eliminate technical errors (**Table 17**).

Table 17 Haplotype obtained from six lambs from the same sire, G173. An asterisk (*) symbol shows that there was suspected error for assignment of DQB2 allele for lamb, y006. The sequence was then re-examined.

Sire	Lamb	DRB1	DQA1	DQA2	DQA2-like	DQB1	DQB2
G173	y005	G2	Null	AY312375	AY312394	Null	AJ238946
	y006	G2	Null	AY312375	AY312394	Null	AJ238941*
	y019	G2	Null	AY312375	AY312394	Null	AJ238946
	y020	G2	Null	AY312375	AY312394	Null	AJ238946
	y023	G2	Null	AY312375	AY312394	Null	AJ238946
	y030	G2	Null	AY312375	AY312394	Null	AJ238946

2.5.3 Re-examination of Null Alleles

Null allele can often result from PCR errors. To solve this problem the pedigree and haplotype data were used for confirmation. For example, **Table 18** shows the problem, which indicates the sample 100t022 poses errors of a false positive null for DQA1 and DQB1 genes. Null alleles could also be due to a point mutation at a primer binding site (Mikko et al. 1999), this problem could be solved by using an additional set of primers (Ballingall & Tassi 2010). Examples of this problem shall be discussed in details in research chapters later.

Table 18 Lamb haplotypes obtained from the same sire, 8t055 by the SORT BY programme. An asterisk (*) symbol showed there was an error of null for DQA1 and DQB1 genes for lamb, 100t022. The DQA1 and DQB1 retyping process were redone for that particular DNA sample (100t022).

Sire	Lambs	DRB1	DQA1	DQB1	DQA2	DQB2
8t055	100t022	GSF	Null*	Null*	AY312387	N_all3
	100t023	GSF	HE574809	GU191460	AY312387	N_all3
	100t032	GSF	HE574809	GU191460	AY312387	N_all3
	100t032	GSF	HE574809	GU191460	AY312387	N_all3
	100t034	GSF	HE574809	GU191460	AY312387	N_all3

2.6 Submission of Alleles to the Databases

2.6.1 European Bioinformatics Information (EBI)

Novel alleles were submitted to the EBI database. Firstly, the sequences were prepared according to the standard guidelines as described in the EBI website. Confirmation was required that primer sequences were not included in sequences submitted. The identification of 5' and 3' coding sequence location numbers (start and stop codon) was determined from the sequences. All alleles submitted from this study are listed in **Appendix 5**.

2.6.2 Immuno Polymorphism Database (IPD)

The IPD is the specific databases for polymorphic genes related to immune system. One of specific databases in this system is IPD-MHC which consists of MHC sequences from different species. This database acts as a centralised resource for those working the same MHC area.

The requirements for submission of alleles in the sheep IPD-MHC are available in the IPD-MHC website (<https://www.ebi.ac.uk/ipd/imgt/hla/subs/submit.html>). Briefly, prior to this submission, the novel sequences must be accepted in the EBI or NCBI database. In addition, only sequences that consist of the full sequence of exon 2 are acceptable. Thus, only selected sequences which amplified the whole exon 2 were submitted to IPD database in this study.

2.7 Statistical Analysis

The procedures on the SAS suite of statistical programs version 8.2 (SAS Institute, Cary, North Carolina) were used.

2.7.1 Allele Frequencies

Allele frequencies were computed using the **ALLELE** procedure on SAS/Genetics statistical package. This procedure has been chosen because it delivers maximum likelihood estimates of allele frequencies with the nonexistence of recessive genes (Stear et al. 2005).

2.7.2 Association between MHC class II Haplotypes with FECs

FECs were transformed to $\ln(\text{FEC} + 1)$ before the analysis. This is to correct heterogeneity of variance and also produce approximately normal distribution. The association between haplotypes and nematode resistance were made with a **MIXED** procedure on the SAS.

2.7.3 Linkage Disequilibrium

Linkage disequilibrium was determined by the **ALLELE** procedure in SAS. In this study, two linkage disequilibrium measures for each pair of alleles at Ovar-DRB1, DQA1, DQA2 (DQA2-like), DQB1, DQB2 and DQB2 were determined. This measure includes the correlation coefficient (r) and Lewontin's (D').

2.8 Phylogenetic Analysis

Neighbour-joining trees (Saitou & Nei, 1987) were built on the basis of genetic distance, estimated by Kimura's (1980) two-parameter method, using Molecular Evolutionary Mega5 (<http://www.megasoftware.net>). The reliability of the trees was estimated by bootstrap confidence values (Felsenstein, 1985).

CHAPTER 3

GENETIC DIVERSITY OF OVAR-DRB1 IN TEXEL

3.0 Summary

Ovar-DRB1 polymorphisms have been noted to influence resistance to infectious disease. Thus, many attempts have been made to characterize the genetic diversity of Ovar-DRB1 in different breeds of sheep. A population-based study in Ireland determined Ovar-DRB1 Texel profiles by using sequence-based typing. We aimed to extend the characterization of the genetic diversity Ovar-DRB1 using the same approach on another flock. A total of 235 Texel DNA samples were tested. 18 distinct Ovar-DRB1 different alleles were detected in this study. The alignment of 18 exon 2 of Ovar-DRB1 revealed the existence of 27 amino acid polymorphic sites, eleven of which (β 12, β 26, β 37, β 38, β 56, β 60, β 66, β 67, β 70, β 74, β 86) are highly polymorphic with three amino acid substitutions. Four amino acid substitutions were found at the two amino acid sites (β 57 and β 71). At one of the sites, β 11, five amino acid substitutions were observed. The most prevalent alleles were M and G2 in Texel. The 'A' allele was found distinct from the rest of Texel DRB1 alleles. The high level of sequence polymorphisms detected from this study demonstrates the extensive diversity of Ovar-DRB1. The results also supported the fact that sequence-based typing with multiple primers is an efficient typing method of Ovar-DRB1 in sheep.

3.1 Introduction

DR molecules are made up of α and β chains. The DRA gene encodes the α chain of the DR molecule. On the other hand, the DRB gene encodes the β chain of the same molecule. There are four DRB loci in sheep (Dukkipati et al. 2006b). However, only one of the four is a functional gene namely DRB1, and the remaining three are pseudogenes, DRB2, DRB3 and DRB4. The pseudogenes lack exon 1 and 2 (Dukkipati et al. 2006b). Ovar-DRB1 is one of the MHC class II genes that are polymorphic (Ballingall et al. 2011).

Characterizing diversity of DRB1 exon 2 is an area of particular interest for many researchers as this region is important in encoding glycoprotein dimers (Fremont et al. 1996). Earlier studies have sequenced DRB1 exon 2 in Scottish Blackface (Schwaiger et al. 1995), Latxa and Karrantzar (Jugo & Vicario, 2000) Finnish and Russian (Kostia et al. 1998), Texel (Sayers et al. 2005b), Coopworth, Suffolk, and Cheviot (Konnai et al. 2003). Today, there are more than 100 catalogued sheep DRB1 allele sequences in the GenBank database. Multiple approaches have been reported to describe the diversity of the DRB1 locus in sheep. These include PCR-RFLP, PCR-SSCP, length polymorphisms of microsatellite in intron 2 together within exon 2 and sequence-based typing (reviewed by Dukkipati et al. 2006). Sequence-based typing is thought to be efficient compared with other methods because it is sufficiently sensitive to capture single-base mutations (Ballingall & Tassi 2010).

Texel is one of the most important sheep breeds in the UK and are known to be resistant against nematodes (Bishop et al. 2004). A previous study by Sayers et al. (2005) has examined the genetic diversity of DRB1 in a Texel flock in Ireland. Their work showed extensive polymorphisms of DRB1 by means of sequence-based typing. Although Texel sheep have been characterized from that previous study, it is interesting to determine the variation of DRB1 in other populations. This study therefore, explores the genetic diversity of DRB1 with approximately 235 samples from Texel breed using sequence-based typing.

3.2 Materials and Methods

3.2.1 Sheep and DNA Source

A total of 235 Texel lambs were studied from Roslin Institute's Blythbank farm in the Scottish Border region. The flock has consistent pedigree records. They had been collected for a previous study by Bishop et al. (2004). The lambs were sampled (blood and faeces) on three occasions each, July, August and September (lambs were 5, 6 and 7 months old) in 1998-2000 (Bishop et al. 2004). Genomic DNA for use in PCR amplification was isolated from the buffy coat using a DNA extraction kit (Qiagen, Germany) as was described in **Chapter 2**.

3.2.3. Primers

Genomic DNA amplification of Ovar-DRB1 alleles was performed using two sets of locus-specific primers (see **Table 19**). The primers and their positions relative to the second exon are illustrated in **Figure 6**. The first set of primers, ERB3 and SRB3 (Konnai et al. 2003) was positioned in the flanking regions of the exon 2, while the second set of primers, DRB1_27F and DRB1_27R (Ballingall et al. 2008) was positioned in introns 1 and 2 respectively. The use of the second set of primers was to cover the whole of exon 2, to validate alleles amplified by the first set of primers and to check homozygotes or null allele.

3.3.4 Amplification and Sequencing of Ovar-DRB1 gene

For the PCR reaction, 1µl of the DNA containing solution was added to 20µl of the PCR master mix as described in **Chapter 2** (using 0.5U Taq DNA polymerase (Qiagen), 0.5 µM of each primer, 25 mM of MgCl² (Qiagen), 150 µM dNTP (dNTPs Invitrogens). PCR amplification was carried out on a thermal cycler (Gene Amp-PCR system2700 Version2.0- Bio systems A&B). Negative controls consisting of samples without DNA were run in for each PCR. The PCR reaction used and the band sizes amplified by ERB3/SRB3 and DRB1_27F/DRB1_27R are shown in **Table 19**.

Table 19 PCR primers for amplification of the second exon of the Ovar-DRB1 gene. Amplicon size includes the primer sequences.

Primer Name	Primer Position*	Direction	Primer Sequence	Amplicons sizes (bp)	Number of Cycle	Reaction conditions
ERB3	6677-6698	F	5'-CTC TCT CTG CAG CAC ATT TCC T-3'	276	32	94°C for 2 min, then 94°C for 30 s, 61°C for 30 s, 72°C for 30 s, 72°C for 5 min
SRB3	6936-6953	R	5'-CGC TGC ACA GTG AAA CTC -3'			
DRB1_27F	6634-6953	F	5'-ATT AGC CTC TCC CCA GGA GTC-3'	368	32	95°C for 2 min, then 95°C for 60 s, 60°C for 60 s, 72°C for 60 s, 72°C for 5 min
DRB1_27R	6983-7002	R	5'-CAC ACA CAC ACT GCT CCA CA-3'			

*Primer position refer to AM884913 sequence reported by Ballingall et al. (2008)

3.3 Results

3.3.1 Sequence Polymorphism of the Exon 2 Ovar-DRB1

The sequencing was initially performed with ERB3 and SRB3 primers by which 276 bp were amplified. The amplification did not cover the whole of exon 2. Using the second primer set (DRB1_27F and DRB1_27R), the whole exon 2 and adjacent intron sequences were amplified (368bp). 18 distinct sequences were identified from the 235 Texel sheep (**Table 20**) and no novel alleles were determined as all alleles had already been reported in the database.

Table 20 Nomenclature of Ovar-DRB1 alleles detected in Texel

Local name	Accession number	IPD name
A	FN543119	DRB1*0901
B2	FN543117	DRB1*0601
C2	AM884914	DRB1*0401
D2	FM209040	DRB1*1601
DQ659115	DQ659115	DRB1*1501
FM998807	FM998807	DRB1*0308
FN393738	FN393738	DRB1*1202
FN543114	FN543114	DRB1*0201
FN870432	FN870432	DRB1*0805
FR686849	FR686849	DRB1*2202
G2	AB017206	DRB1*1101
GSF	AY227049	DRB1*1401
H3	AM885929	DRB1*0102
HG515541	HG515541	DRB1*0406
L	AM884913	DRB1*0302
M	U00212	DRB1*0201
TUV	KC733423	DRB1*0701
U00219	U00219	DRB1*2002

There were considerable nucleotide variations and corresponding amino acid variation among DRB1 alleles found in Texel sheep. 55 of the 237-nucleotide sites (23.2 %) analysed in this study showed variability (**Figure 7**). An alignment of the deduced amino acid sequence encoded by exon 2 is shown in **Figure 8**. Twenty-six (33.3%) amino acid polymorphic sites were identified. Most variables were found in amino acid residues β 12 (K, R, T), β 26 (F, L, Y), β 37 (F, T, Y), β 38 (A, L, V), β 56 (P, Q, R), β 60 (H, Q, Y), β 66 (D, E, N), β 67 (I, L, F), β 70 (Q, R, S), β 74 (A, E, N) and β 86 (F, G, I) with three different amino acids per site, and in residues β 57 (A, D, E, S) and β 71 (A, K, T, R) with four, and five different amino acid per site at β 11 (A, H, S, T, Y) was observed. All polymorphic amino acid sites that were included in the peptide-binding region were polymorphic (**Table 21**).

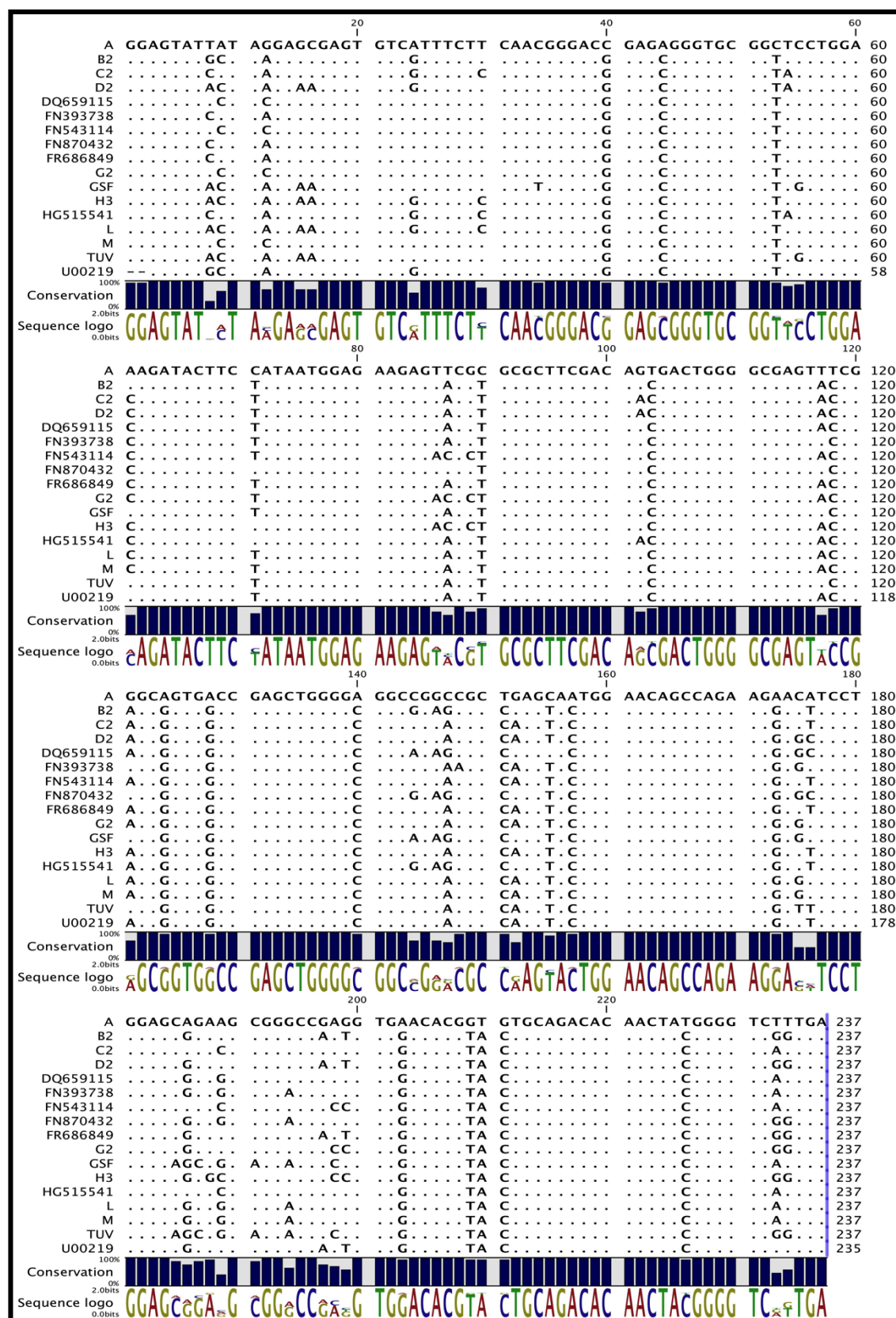


Figure 7 Nucleotide sequences of the second exon of Ovar-DRB1 alleles found in Texel.

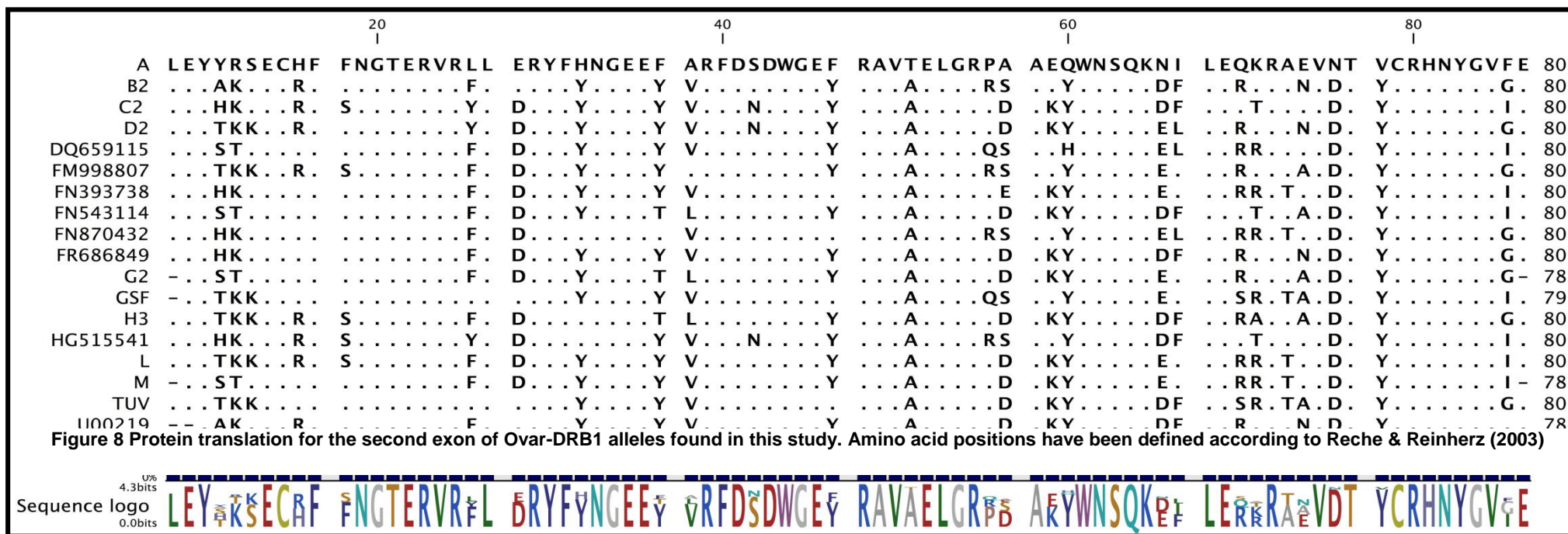


Table 21 Amino acid variations in Texel in this study Vs published sheep DRB1 alleles. Amino acid positions involved in the antigen binding sites (according to Reche & Reinherz (2003) are indicated by grey background; novel amino acids found in this study are indicated in blue, while amino acids that were only found in previous studies are given in red.

Amino Acid Position	Texel	Previously Published
11	A, H, S, T, Y	A, D , H, R , S, T, Y
12	K, T, R	K, T, R
13	K, S	K, R , S
16	H, R	H, R
18	F, S	F, S
26	F, L, Y	F, L, Y
28	D, E	D, E
32	H , Y	F , Y
33	N	H , T , Y
37	F, T, Y	F, N , T, Y
38	A, L, V	A, L, V
42	N, S	N, S
47	F, Y	F, Y
51	A, T	A, T
56	P, Q, R	P, Q, R
57	A, D, E, S	A, D, E, S
59	E, K	E, K
60	H, Q, Y	H, Q, Y
66	D, E, N	D, E, N
67	F, I, L	F, I, L
70	Q, R, S	Q, R, S
71	A, K, R, T	A, K, R, T
73	A, T	A, T
74	A, E, N	A, E, N
76	D, N	D, N
78	V, Y	V, Y
86	F, G, I	D , F, G, I, V

3.3.2 Frequencies of the Ovar-DRB1 Alleles

The frequencies of the DRB1 alleles detected in this study are shown in **Table 22**. The allele frequencies ranged from 0.2 to 21.5%. The most frequent alleles in Texel were M and G2 (21.5 and 20.4% respectively). There was a short tail of low frequency alleles. Four alleles namely DQ659115, FM998807, FN393738 and FN870432 were present in less than 1% of chromosomes.

Table 22 Ovar-DRB1 alleles and their frequencies found in Texel

Allele	Number	Frequency (%)	SE	Texel	
				95 CI (%)	
				Lower	Upper
A	31	6.60	1.18	4.26	9.15
B2	15	3.19	0.85	1.70	4.89
C2	5	1.06	0.47	0.21	2.13
D2	59	12.55	1.62	9.36	15.74
DQ659115	4	0.85	0.42	0.21	1.70
FM998807	2	0.43	0.30	0.00	1.06
FN393738	2	0.43	0.30	0.00	1.06
FN543114	6	1.28	0.51	0.43	2.34
FN870432	1	0.21	0.21	0.00	0.64
FR686849	8	1.70	0.59	0.64	2.98
G2	96	20.43	1.76	17.02	23.62
GSF	37	7.87	1.19	5.53	10.43
H3	62	13.19	1.59	10.00	16.17
HG515541	5	1.06	0.47	0.21	2.13
L	18	3.83	0.92	2.13	5.53
M	101	21.49	1.83	18.09	25.11
TUV	8	1.70	0.59	0.64	2.77
U00219	10	2.13	0.66	0.85	3.40

3.3.3 Phylogenetic analysis among of the Ovar-DRB1 Alleles

A phylogenetic analysis of the 18 Ovar-DRB1 Texel was also conducted. **Figure 9** shows that A allele was separated from the rest of alleles, while, DQ659115 and FN870432 are grouped in separate clusters from all other alleles.

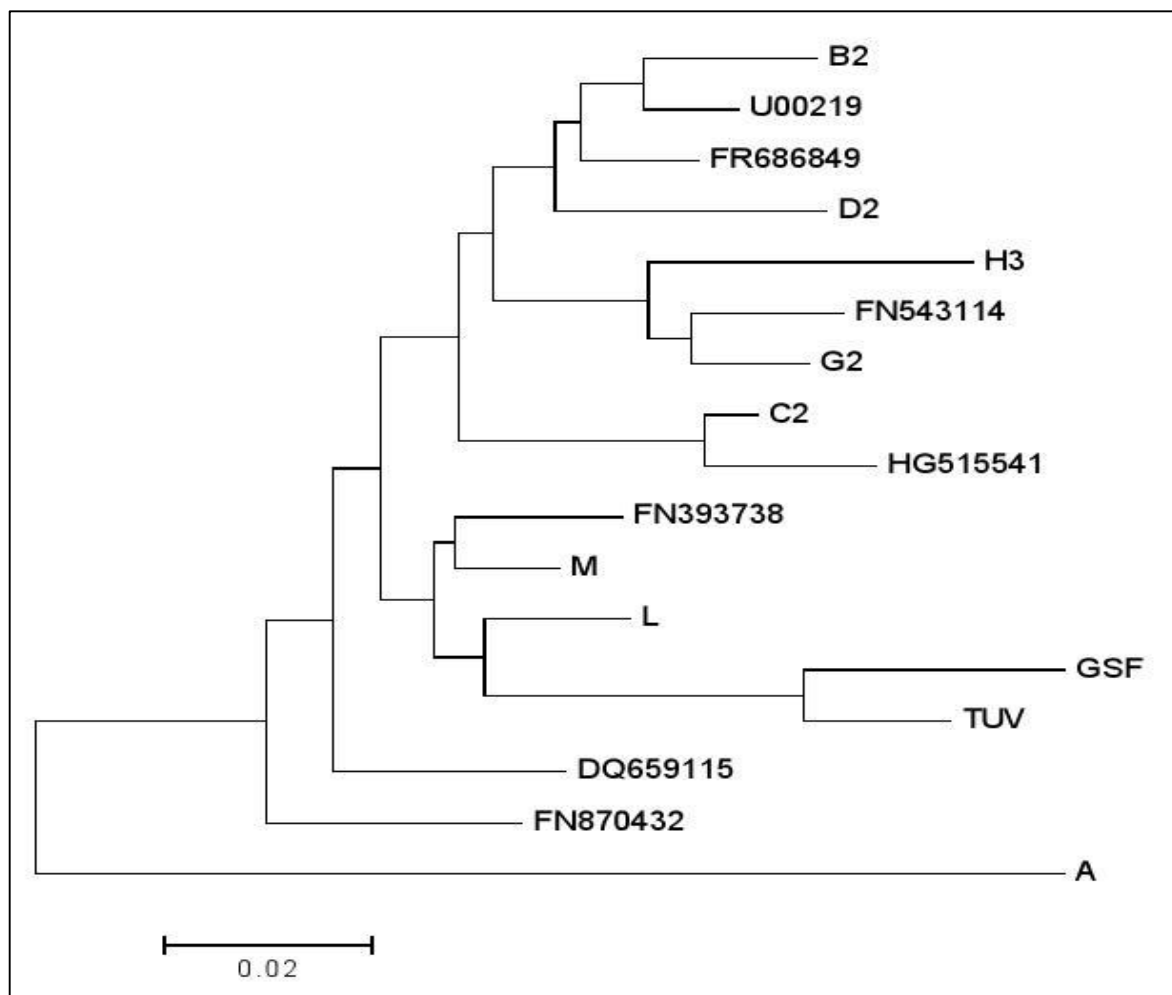


Figure 9 A neighbor phylogenetic tree constructed from exon 2 sequences of DRB1 gene from Texel in this study. The number at the forks indicates the bootstrap confidence values and branch lengths are proportional to genetic distance.

3.4 Discussion

The main objective of the current study was the characterization of exon 2 DRB1 gene polymorphism in a sample of Texel. Sequence-based typing with two set of primers together with haplotype checking were used to allow accurate typing of the Ovar-DRB1 locus from Texel DNA. Sequencing of the exon 2 DRB1 DNA revealed a 237 bp nucleotide encoding a 79 amino acid protein. From Texel, 18 alleles with no novel alleles were identified. No insertion or deletion from DRB1 sequences were found in this study. The A or Ovar-DRB1*0901 was an outgroup from the rest of alleles.

Sequence-based typing based on the two oligonucleotide primers; ERB3/SRB3 and DRB1_27F/DRB1_27R were used in this Texel population. The first set of primers was able to amplify all alleles and inclusion of all polymorphic sites. However, the primer amplified a partial region of exon 2. Our interest was to detect the whole of exon 2, as this exon forms the MHC class II with the DRA allele. The use of the second set of primers located in introns covered the whole exon 2. In addition, the second set of primers in this study also enabled us to validate the results obtained from the first primer set especially the homozygous samples (Ballingall & Tassi 2010).

There was a total of 18 alleles detected from 235 Texel. No new alleles were found as all alleles had been reported previously. The number of alleles detected for the Ovar-DRB1 locus is lower than that for the Suffolk DRB1 (28 alleles; n=71); Konnai et al. 2003b), but higher than that for DRB1 in Cheviot and Corriedale sheep (14 alleles; n=20 and 9 alleles; n=6); Konnai et al. 2003b). It was also interesting to note that the number of alleles in the Texel population in this study was higher than in the Texel population studied by Sayers et al. (2005b) who, using the same technique, only identified eight alleles (n= 179). This remarkable difference in the number of alleles probably as result of the different number of sampled between the farms.

Among 18 alleles detected, three common alleles (AY227049, U00212 and AB017206) were shared between this study and Sayers et al. (2005). In the Texel population examined here, the DRB1*1202 (FN393738) allele was present. DRB1*1202 allele was thought to be a common allele in domestic sheep (Herrmann et al. 2005). Beside Ovar-DRB1*1202, other alleles such as DRB1*0203, 0404, 0801 and 1101 are typically

present in sheep of Spanish and English decent in the USA (Herrmann et al. 2005) of which two were detected in the Texel.

The most frequent allele in this Texel flock was DRB1*0201 or M, followed by DRB1*1101 or G2. This finding was different compared with Sayers et al (2005), who found the GSF (AY227049) is common allele in the same breed. Earlier studies demonstrated that the DRB1*0702 has been reported frequently as the most common allele in multiple breeds (Jugo & Vicario 2000; Konnai et al. 2003; Larruskain et al. 2010).

Among the alleles detected in this Texel population, DRB1*0901 allele stood out because of its location in the topology of the tree, being an outgroup from the rest of other DRB1 alleles in this study. Similarly, the allele appeared distinct from the other alleles from 15 full-length Ovar-DRB1 sequences in Ballingall et al. (2008) study. The finding in this study supports the 09 family of sequence as a divergent family of alleles at the Ovar-DRB1 locus.

3.5 Conclusion

This chapter reports the allelic distribution of the Ovar-DRB1 gene in Texel using sequence-based typing. The study has found a high rate of polymorphism and diversity, our results thereby adding to the knowledge of the genetic diversity of the Ovar-DRB1 gene in Texel breed. This chapter also demonstrated that the sequence-based typing with two primers is sufficient to amplify the Ovar-DRB1 alleles in the breed studied.

CHAPTER 4

GENETIC DIVERSITY OF OVAR-DQA1 IN TEXEL

4.0 Summary

Previous studies have established the genetic diversity of DQA1 gene in various breeds of sheep. However, the genetic diversity of DQA1 has yet to be described in Texel. In this study, using 235 Texel DNA samples, Ovar-DQA1 gene in Texel is characterized by sequence-based typing. Nine Ovar-DQA1 alleles were identified and the alignment of exon 2 of Ovar-DQA1 revealed the existence of 26 amino acid polymorphic sites, eight of which ($\alpha 18$, $\alpha 52$, $\alpha 53$, $\alpha 55$, $\alpha 56$, $\alpha 72$, $\alpha 75$ and $\alpha 79$) are highly polymorphic with at three amino acid substitutions. Four amino acid substitutions were discovered at the two amino acid sites ($\alpha 68$ and $\alpha 69$). The DQA1 allele was M33304 with a frequency of 41% in this population. The DQA1 null allele was observed with a frequency of 22%, making it the second most common DQA1 allele in this study. The majority of Ovar-DQA1 sequences are on the same main branch of the phylogenetic tree as goat DQA1 compared to the cattle DQA1. The results suggested that extensive polymorphism reported in Texel are consistent with polymorphisms reported in a previous investigation DQA1 in other breeds. The work also has established the sequence-based typing system in Ovar-DQA1.

4.1 Introduction

The MHC genes are the most polymorphic loci in the genome of the mammal. The function of these genes is encoding of MHC molecules, a vital immune component, also functioning as a presenter of processed peptide antigens to adaptive immune response (Trowsdale et al. 1993). Sheep MHC express only two classes of class II proteins, DR and DQ, and both are seen to be important for priming CD4⁺ T cells specific for many different pathogens. The DR molecules are encoded by DRB1 gene while DQ molecules are encoded DQA and DQB genes (Dukkipati et al. 2006b).

Sheep possess two distinct types of DQA loci composing of DQA1 and DQA2 (Hickford et al. 2007). It was shown that DQA1 null or absence of DQA1 gene in sheep is associated with DQA2-like (Hickford et al. 2004). Ovar-DQA1 is known to be functional (Ballingall et al. 2015) and has been extensively sequenced (Zhou & Hickford, 2004; Ballingall et al. 2015) and shown to be a highly polymorphic gene. To date, more than 20 DQA1 alleles have been reported (Zhou & Hickford, 2004; Ballingall et al. 2015). In order to increase knowledge on the DQA1 genetic diversity in sheep, we investigated the DQA1 genetic diversity in Texel. The study also highlighted the development of sequence-based typing system for the Ovar-DQA1 locus. Furthermore, allele frequencies of DQA1 in Texel sheep are presented together with the evolutionary relationship between DQA1 alleles in ruminants.

4.2 Materials and Methods

4.2.2 Primers

Four locus-specific primers, DQA1-up/DQA1-down (Zhou & Hickford, 2004), NikDQA1F/NikDQA1R, 92.y085F/92.y085R and Z28518F/Z28518R were used in this study (**Table 23**). The primers and their positions relative to the second exon are illustrated in **Figure 10**. The DQA1-up/DQA1-down and NikDQA1F/NikDQA1R primers were designed based on sequence from M33304 (Scott et al. 1991a). The primer pair of DQA1-up/DQA1-down was positioned in the flanking region of the exon 2. While, the second primer pair of NikDQA1F/NikDQA1R was positioned in intron 1 and 2, thus, the amplified sequences from the later primers covered the whole exon

2Ovar-DQA1. By using these two sets of primers, most of the DQA1 allele were identified except 92.y085 and Z28518 alleles in a small proportion of samples. These were detected upon haplotype analysis. The allele-specific primers, 92.y085F/92.y085R and Z28518F/ Z28518R were designed and use of both primers enabled the amplification of the 92.y085 and Z28518 alleles.

4.2.3 Amplification and Sequencing of exon 2 of Ovar-DQA1 gene

For the PCR reaction, 1µl of the DNA was added to 20µl of the PCR master mix as described in **Chapter 2**. Negative controls consisting of samples with water instead of DNA were run in each PCR. The PCR reaction used and the band sizes amplified by the four sets of primers are shown in **Table 23**. A novel allele was cloned into the pGEM-T-easy vector and was validated by cloning and sequence analysis.

Table 23 The PCR primers for amplification of the second exon of Ovar-DQA1 gene. Amplicon size includes the primer sequences.

Primer	Primer Location	Direction	Primer Sequence*	Amplicon size (bp)	Number of Cycles	Reaction conditions
DQA1-up	348-367	F	5'-ACCTGACTC AcC TGA CCA CA -3'	268	32	94°C for 2 min, then 94°C for 30 s, 61°C for 30 s, 72°C for 30 s, 72°C for 5 min
DQA1-down	594-616	R	5'- AACACATACTGTTGGTAGCAGCA -3'			
NikDQA1F	251-274	F	5'-ACTGGCCACAAATGAAGCCCACAA-3'	477	32	94°C for 2 min, then 94°C for 30s, 61°C for 30 s, 72°C for 30 s, 72°C for 5 min
NikDQA1R	753-776	R	5'-AGAAGGCAGAAGATGAGGGTTCAG-3'			
92.y085F	348-365	F	5'- CTCCGACTCAGCTGACCA-3'	270	32	94°C for 2 min, then 94°C for 30s, 61°C for 30 s, 72°C for 30 s, 72°C for 5 min
92.y085R	594-616	R	5'-AACACTTACTGTTGGTAGCAGCA -3'			
Z28518F	348-367	F	5'-CCCTGACTCAGCTGACCACA-3'	268	32	94°C for 2 min, then 94°C for 30s, 61°C for 30 s, 72°C for 30 s, 72°C for 5 min
Z28518R	594-616	R	5'-AACACTTACTGTTGGTAGCAGCA -3'			

*The primer positions refer to Ovar-DQA1 sequence M33304 reported in Scott et al. (1991a).



Figure 10 Diagrammatic representation of the second exon and immediate flanking region of Ovar-DQA1 (M33304 sequence) showing the location and direction of primers detailed in Table 24.

4.2.4 Nomenclature

Throughout this chapter, gene accession number was adopted as all sequences were not yet accepted by the IPD-MHC database yet. All new sequences were submitted to the EBI database and assigned with the accession number.

4.2.5 Phylogenetic Analysis

A compilation of a representative number of sheep, cattle and goat DQA1 sequences was made (**Appendix 3**). The GenBank accession numbers of the sequences for phylogenetic analysis were: the sheep DQA1 sequences found in this study (**Table 24**) and from other studies AF276954, AF317617, AY229894, AY230209, AY230210, AY265308 and Z28420 (Zhou & Hickford 2004) HG798783–HG798798 (Ballingall et al. 2015); the cattle DQA1 sequences: AB257101-13, AB259566-77 (Takeshima et al. 2007), the goat DQA1 sequences: AY464656-57, AY665664-66 (Amills et al. 2005). The tree was rooted with the human DQA1 sequence HLA-DQA1*0101 (L34082; Yasunaga et al. 1996) as an out group. A neighbour-joining tree (Saitou & Nei, 1987) was constructed on the basis of genetic distances, estimated by the Kimura (1980) two-parameter method, using the MEGA 6.0 program (Tamura et al. 2013). Relative support of the branching order was determined using bootstrap analysis with 1000 iterations. Identical sequences with different GenBank number were identified before the analysis. In addition, GenBank sequences were trimmed to the length corresponding to the PCR amplimers before generating the neighbour-joining tree.

4.3 Results

4.3.1 Sequence Polymorphism of the Second Exon of Ovar-DQA1

A total number of 235 Texel DNA samples were genotyped for Ovar-DQA1. Using four sets of primers, a total of eight different Ovar-DQA1 sequences were identified from the Texel population in this study (**Table 24**). Using the first set of primers, DQA1-up/DQA1-down, eight different Ovar-DQA1 sequences have been determined. However, the first primer set did not amplify the whole of exon 2. In order to obtain complete exon 2 sequences, we designed a second set of primers NikDQA1F/NikDQA1R, which are located within intronic sequences (intron 1 and intron 2). With the second set of primers, the whole of exon 2 part of intron 1 and 2 was successfully amplified. However, upon haplotype analysis, we detected two specific alleles, 92.y085 and Z28518 which occasionally did not amplify in some heterozygous samples. Thus, the specific allele primers were designed (primer sets Z28518F/Z28518R and 92.y085F/92.y085R). All samples with no detection of 92.y085 and Z28518 alleles were identified and the specific allele primer PCR reaction managed to amplify those two alleles. Using four sets of primers, all DQA1 alleles were identified. Under the established conditions, a total of eight Ovar-DQA1 different sequences have been identified from the Texel population in this study.

Table 24 Nomenclature of the Ovar-DQA1 exon 2 detected in Texel and comparison with those previously described.

Local name	Accession number	Identical to
extendedHE574809	LN827890	AF276954, HE574809, HG798787
extendedZ28518	LN827891	Z28518
extendedAY265308	LN827893	AY265308
extendedZ28418	LN827894	Z28418
extendedHQ728659	LN827895	HQ728659, Z28420
M33304	M33304	NA
92.y085	LN736359	NA
8t036	LN827892	AF276956

There is variation of nucleotide and deduced amino acid between eight DQA1 alleles found in Texel sheep. 51 of the 246-nucleotide sites (20.7%) analysed in this study presented variability (**Figure 11**). An alignment of the deduced amino acid sequence encoded by exon 2 is shown in **Figure 12**. Twenty-six (31.7%) amino acid polymorphic sites were identified. In general these polymorphism were clustered into three separate areas that were assigned I, II and III (I: 9-18, II: 47-56, III: 66-79). Most variables were found in amino acid residues $\alpha 10$ (A, I, T), $\alpha 18$ (K, S, T), $\alpha 50$ (E, M, V), $\alpha 53$ (E, K, Q), $\alpha 55$ (G, R, T), $\alpha 56$ (R, S, Y), $\alpha 72$ (N, S, T), $\alpha 75$ (I, L, V) and $\alpha 79$ (D, M, R) with three different amino acids per site, and in residues $\alpha 68$ (A, S, T, V) and $\alpha 69$ (A, F, G, V) with four. The comparison of amino acid variations between this flock study and published DQA1 sequences can be viewed in **Table 25**. We determined that the Texel breed in this study had similar polymorphisms to what has been previously described in Ovar-DQA1 (Zhou & Hickford 2004; Ballingall et al. 2015). The sites in Texel had one or more different amino acids not represented in previously described polymorphic amino acid positions of Ovar-DQA1.

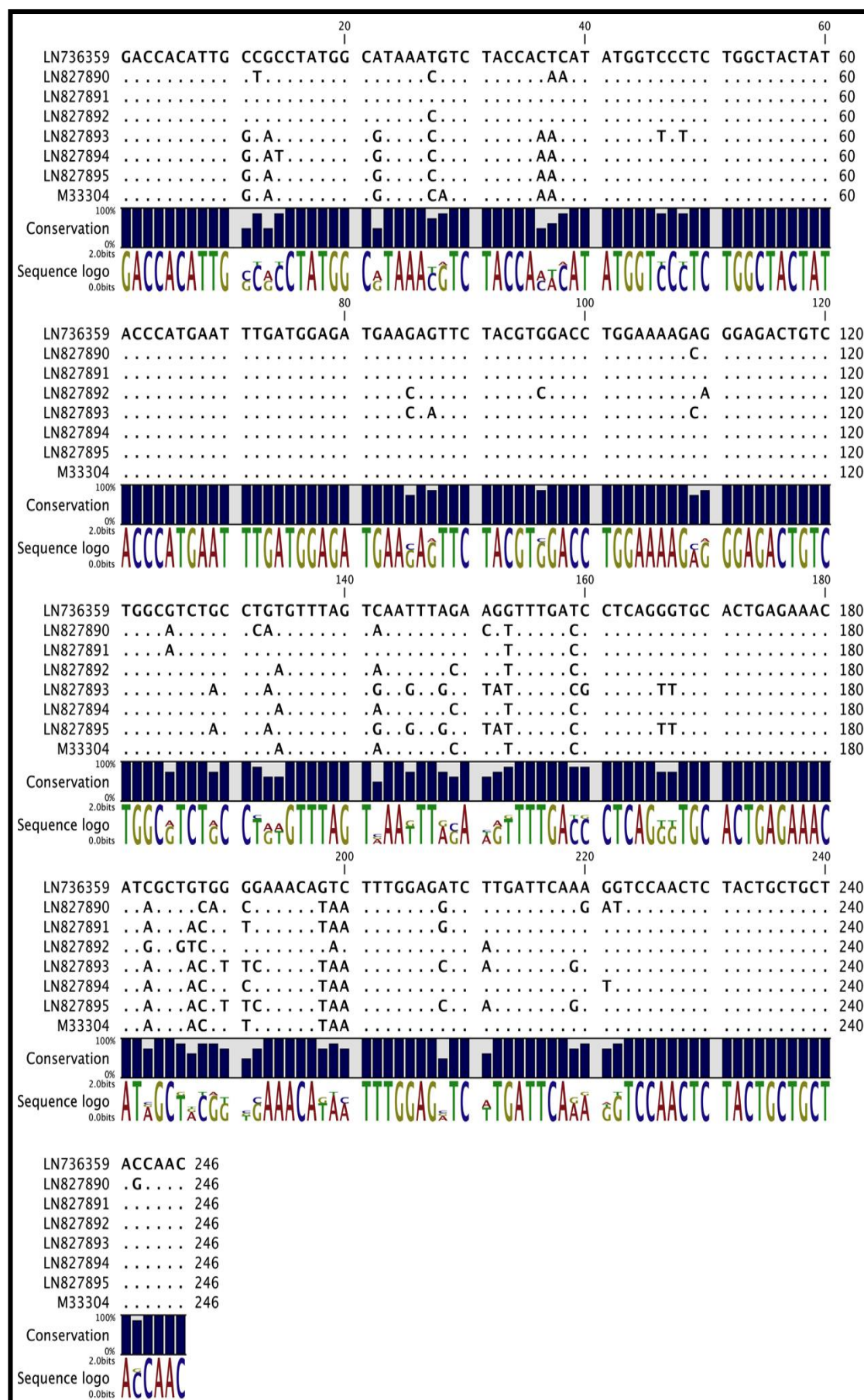


Figure 11 Nucleotide sequence of the second exon of Ovar-DQA1 alleles found in this study. The local allelic nomenclature is used. A dash indicates identity with the top sequence.

Table 25 Amino acid variation in Texel in this study Vs published sheep DQA1 alleles: novel amino acids found in this study are indicated in blue. Amino acids that were only found in previous studies are given in red.

Amino Acid Position	Texel	Previously Published
9	A, G	A, G
10	A, I, T	A, I, T
13	I, V	I, V
15	I, V	I, V
17	H, Q	H, Q
18	K, S, T	K, S, T
21	P, S	S
25	Y	F, Y
34	E, Q	E, Q
36	Y	H, Y
42	K, R	K, R
47	H, R	H, R
50	E, M, V	E, M, V
53	E, K, Q	E, K, Q
54	F, V	F, V
55	G, R, T	A, G, R, T
56	R, S, Y	D, R, S, Y
59	A, P	P
61	F, G	F, G
66	I, M	I
68	A, S, T, V	A, T, V
69	A, F, G, V	A, F, G, L, T, V
71	H, Q	H, Q
72	N, S, T	N, S
75	I, L, V	I, L, V
76	L, M	I, L, M, T
79	D, M, R	D, M, R
86	S, T	S, T

4.3.2 Frequencies of the Ovar-DQA1 Alleles

The frequency of each allele in Texel is shown in **Table 26**. The most frequent DQA1 allele in Texel is M33304 (42.8%) followed by the null allele (22.2%). The rest of the alleles detected were in less than 10%. Rare alleles were detected in less 1% of haplotypes, these were LN827893 and LN827894.

Table 26 Ovar-DQA1 alleles and their frequencies found in Texel flock in this study

Allele	Number	Frequency (%)	SE	95 CI (%)	
				Lower	Upper
LN736359	24	5.11	1.03	3.19	6.81
LN827890	41	8.72	1.24	6.17	11.28
LN827891	32	6.81	1.20	4.68	9.36
LN827892	59	12.55	1.62	9.36	15.76
LN827893	4	0.85	0.42	0.21	1.70
LN827894	5	1.06	0.47	0.21	2.13
M33304	201	42.8	2.36	38.09	47.23
Null	104	22.15	1.83	18.72	25.74

4.3.3 Phylogenetic analysis among of the DQA1 Alleles

Figure 13 illustrates the phylogenetic tree from DQA1 sequences from this study showed that LN736359 and LN827894 are grouped with LN827892 and M33304 respectively. LN827891 and LN82790 alleles are grouped with LN736359 and LN827892. In addition, alleles LN827893 and LN827895 are grouped in a separate cluster.

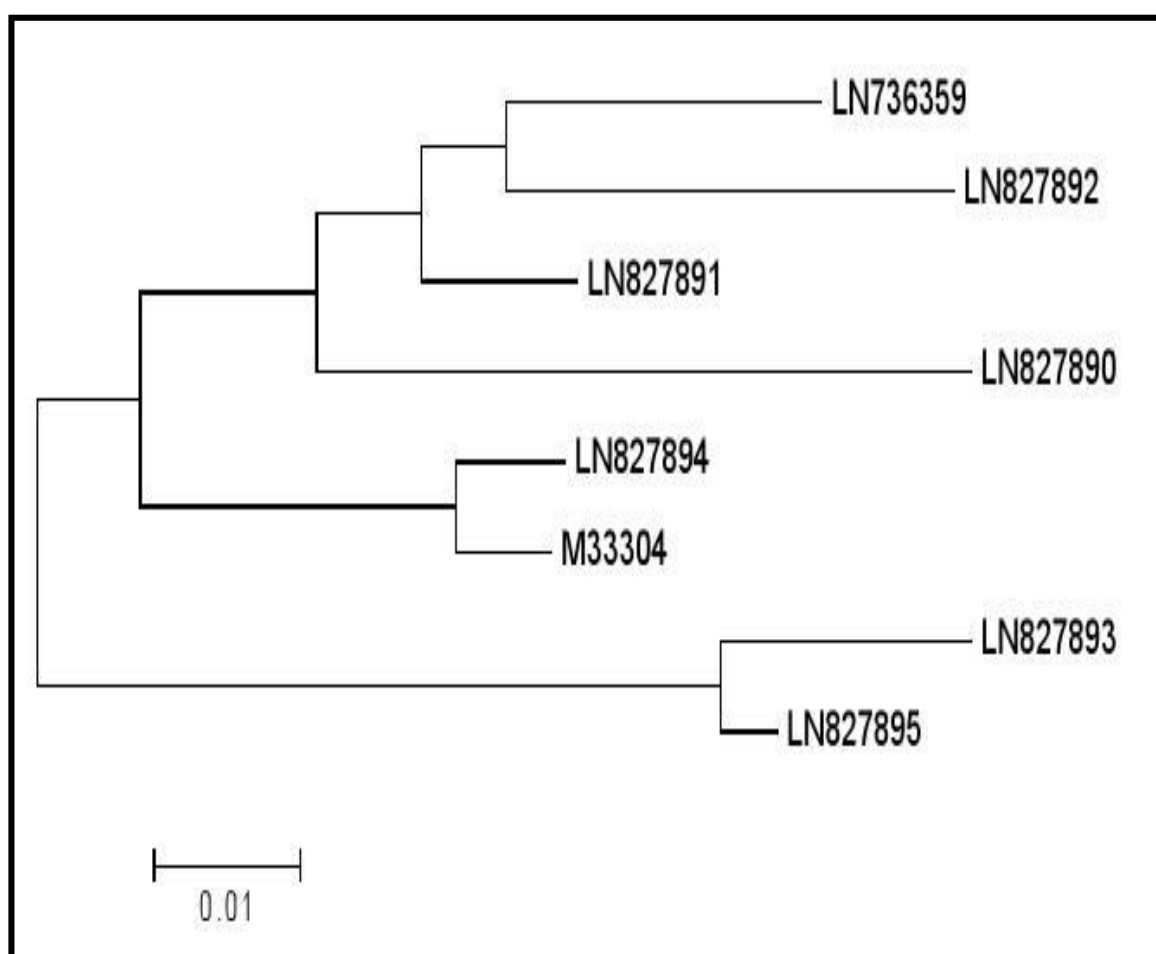


Figure 13 A neighbor phylogenetic tree constructed from exon 2 sequences of DQA1 gene from this study. The number at the forks indicates the bootstrap confidence values and branch lengths are proportional to genetic distance.

A second phylogenetic tree was constructed from exon 2 of the Ovar-DQA1 sequences and the reported cattle DQA1 and goat DQA1 sequences. Some sheep DQA1 alleles sequences clustered with cattle and goat sequences, of which more of sheep Ovar-DQA1 sequences grouped with goat DQA1 (**Figure 14**).

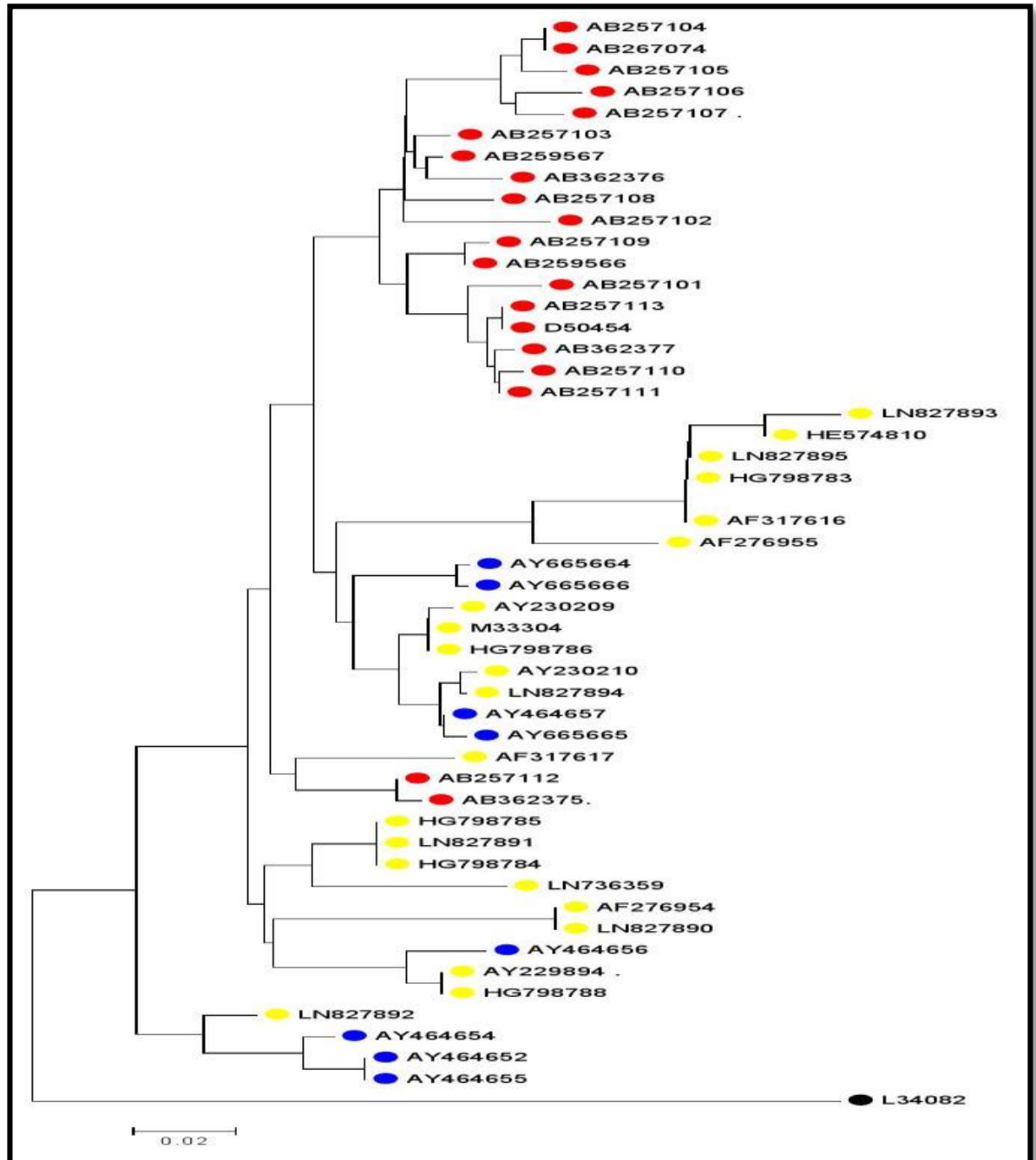


Figure 14 A neighbor phylogenetic tree constructed from exon 2 sequences of DQA1 gene from sheep, cattle and goats. The human DQA1 (L34082) was used as an outgroup. The number at the forks indicates the bootstrap confidence values and branch lengths are proportional to genetic distance. The yellow, red and blue symbols denote Ovar-DQA1, BoLA-DQA1 and Cahi-DQA1 respectively.

4.4 Discussion

The main objective of the current study was the characterization of DQA1 gene polymorphism in Texel sheep. Sequence-based typing of exon 2 revealed a 246 bp nucleotide and encoding an 82 amino acid protein. From Texel, nine distinct alleles were identified including null. No observations of insertion or deletion from DQA1 nucleotide sequences were detected in this study. Four distinct amino acid substitutions were found at two sites. The most frequent DQA1 allele in Texel is M33304 followed by a null allele. Two rare alleles were detected in less than 1% of Texel. Sheep DQA1 sequences clustered more with goat DQA1 than with cattle sequences.

Our main interest is in PCR amplification and sequencing of the complete second exon of DQA1, which encodes the antigen binding site (Dukkipati et al. 2006b). We developed a sequence-based typing method for evaluation of genetic diversity at the Texel DQA1 locus using four primer sets. It was observed that the DQA1-up/DQA1-down primer amplified all alleles effectively; however the amplified sequences did not cover the entire exon 2. To obtain entire exon 2, the primers NikDQA1F and NikDQA1R, which are located in the introns, were designed. Upon haplotype and analysis, it was found that the primers NikDQA1F and NikDQA1R occasionally do not amplify two specific alleles, namely 92.y085 and Z28518 alleles. The problem of preferential amplification of one allele instead of two alleles in heterozygote samples has been described in sequence-based typing (Ballingall & Tassi, 2010). This occurs due to several factors such as difference of GC content between alleles and mismatches between the primer and specific alleles (Walsh et al. 1992). In this study, the problem was resolved by designing additional primers which are allele-specific. The use of additional or multiple primers in the sequence-based typing of DRB1 have been recommended by Ballingall & Tassi (2010).

Based on our knowledge, this study is the first report of Ovar-DQA1 genetic diversity using sequence-based typing method PCR-SSCP approach was previously used to dissect polymorphisms of DQA1 in sheep (Escayg et al. 1996; Snibson et al. 1998; Zhou & Hickford, 2000; Hickford et al. 2007). Hence, we have established the sequence-based typing system in Ovar-DQA1 gene in this study. Nine different sequences (including null) were obtained from sequence analysis of Ovar-DQA1 exon 2 from the

Texel sample. The result found in this study conforms to previous studies that the Ovar-DQA1 is one of a polymorphic locus in MHC class II (Zhou & Hickford 2004; Amills et al. 2005). The population of Texel examined in this study exhibited low variation at the Ovar-DQA1 locus compared with results from a previous sheep study (Zhou & Hickford et al. 2004). They identified 14 alleles in a sample of 300 from six different breeds (Merino, Corriedale, Borderdale, Romney, Awassi, and Finnish Landrace). Thus, the differences in number of alleles in different breeds could be to breed differences or to the relatively small number of samples.

Sequencing of the exon 2 DQA1 DNA revealed a 246 bp nucleotide and encoding an 82 amino acid protein. Large number of amino acid substitutions was observed between alleles. The alignments of DQA1 amino acid sequence analysis revealed that four amino acid substitutions were found at two amino acid sites, $\alpha 68$ and $\alpha 69$. A similar number of substitutions at $\alpha 68$ have also been reported by Amills et al. (2005). Their work suggests that polymorphism at three positions $\alpha 55$, $\alpha 56$ and $\alpha 68$ has been conserved among ruminants due to some vital role. In this study, multiple amino acids substitution was detected at the three positions. This is consistent with expectations.

The null allele was observed with a frequency of 32% thus making it the second most prevalent allele in Texel. To determine whether the animals which appeared null for DQA1 were truly missing the gene or if they were simply failing to amplify it due to mispriming of the oligonucleotides, three main steps have been carried out in this study. Firstly, no PCR product in homozygous null was observed with all primers used. Second, haplotype was used. Thirdly, this confirmation of null is also supported with detection of Ovar-DQA2-like in samples with a null at Ovar-DQA1 (Hickford et al. 2007).

A phylogenetic analysis tree built for DQA1 revealed that sheep alleles were more closely related to goat as compared to cattle alleles. This is in agreement with Zhou & Hickford (2004). These clusters of three ruminant species may arise due to the trans-species hypothesis (Klein 1987), in which ancient sequences that are present in a common ancestor have been retained in several species since their divergence.

4.5 Conclusion

This is the first report of the allelic distribution of Ovar-DQA1 gene in Texel sheep. The study found a high rate of polymorphism and diversity of Ovar-DQA1. This finding has added to current knowledge of the genetic diversity of the Ovar-DQA1. In addition, the study has successfully established sequence-based typing system in Ovar-DQA1.

CHAPTER 5

GENETIC DIVERSITY OF OVAR-DQA2 AND DQA2-LIKE GENES IN TEXEL

5.0 Summary

An in-depth knowledge of MHC genetic diversity is essential for understanding its role in diseases but has yet to be studied in the Texel breed. In this chapter, the Ovar-DQA2 gene was characterized by sequence-based typing using 235 DNA samples. Eight Ovar-DQA2 and one Ovar-DQA2-like alleles were identified. The alignment of nine alleles of Ovar-DQA2 (including the DQA2-like allele) revealed the existence of 25 amino acid polymorphic sites, twelve of which ($\alpha 10$, $\alpha 13$, $\alpha 15$, $\alpha 52$, $\alpha 53$, $\alpha 55$, $\alpha 56$, $\alpha 58$, $\alpha 65$, $\alpha 69$, $\alpha 71$ and $\alpha 79$) had three amino acid substitutions. Four amino acid substitutions were discovered at five sites ($\alpha 14$, $\alpha 61$, $\alpha 64$, $\alpha 68$ and $\alpha 75$). The most prevalent DQA2 allele was AY31275 with a frequency of 23% in this population. The majority of Ovar-DQA2 sequences are on the same main branch of the phylogenetic tree as goat DQA2 as compared to cattle DQA2. In this work, sequence-based typing was applied to capture DQA2 diversity in sheep. The extensive diversity of DQA2 observed in this population is consistent with the diversity reported in other breeds. The result from the DQA haplotype analysis suggests that some Texel sheep have three DQA genes per haplotype.

5.1 Introduction

The class II molecules of the sheep MHC are encoded on the short arm of chromosome 20 in the MHC class IIa region. They are found on the surface of antigen-presenting cells and consist of α and β chains (Dukkipati et al. 2006a). The molecules are associated with regulation of the immune response to infectious diseases. The MHC class IIa region, which encompasses approximately 400kb DNA is subdivided into two regions, DR and DQ (Dukkipati et al. 2006a). The DQ region comprises the DQA and DQB genes (Scott et al. 1991a, b). The DQA region is divided into two loci, DQA1 and DQA2 (Snibson et al. 1998; Hermann-Hoesing et al. 2008). The polymorphisms of Ovar-DQA2 have been defined using RFLP-Southern hybridization (Escayg et al. 1996) and SSCP (Hickford et al. 2004; Ennen et al. 2009; Ballingall et al. 2015). These studies have shown that DQA2 is polymorphic.

The presence of DQA2-like sequences in sheep increases the complexity of MHC DQA diversity (Ballingall et al. 2015). These DQA2-like sequences are characterized by being more similar to cattle DQA sequences as compared with some of DQA2 sheep sequence (Hickford et al. 2004). The DQA2-like sequences may have arisen from ancient interlocus recombination process between DQA1 and DQA2 (Ballingall et al. 2015). The DQA2-like sequences are associated with the null DQA1, thus maintaining two DQA genes per haplotype in sheep (Hickford et al. 2007). So far, the variation of Ovar-DQA2 of Texel sheep has not been reported elsewhere. Therefore in this chapter, we determined the genetic diversity of DQA2 locus in Texels. Here, we also described the development of the sequence-based typing system for DQA2 in sheep.

5.2 Materials and Methods

5.2.1 Primers

The DQA2s-up and DQA2s-down primer pairs used in this study are shown in **Table 27**; **Figure 15** denotes the primer-binding region. The DQA2s-up and DQA2s-down were designed based on two published sequences from M33304 and Z28421 (Hickford et al. 2004). The primer pair of DQA2s-up/DQA2s-down was positioned in the flanking region of the exon 2.

5.2.2 Amplification and Sequencing of exon 2 DQA2

For the PCR reaction, 1µl of the DNA was added to 20µl of the PCR master mix as described in **Chapter 2**. The PCR reaction used and the band sizes amplified by the DQA2s-up and DQA2s-down primers are shown in **Table 27**.

Table 27 PCR primers used for amplification the second exon of Ovar-DQA2 and Ovar-DQA2-like gene in this study.

Primer	Primer Location	Primer Sequence	Amplicons size (bp)	Number of cycles	Reaction Conditions
DQA2s-up	239-261	5'-ACT ACC AAT CTC ATG GTC CCT CT -3'	241	33	94°C for 2 min, then 94°C for 30 s, 63°C for 30 s, 72°C for 45 s.
DQA2s-dn	457-480	5'-GGA GTA GAA TGG TGG ACA CTT ACC -3'			

The primer position refer to Ovar-DQA2 sequence OLA-DQA2*0101 (AY312375) reported in Hickford et al. (2004)

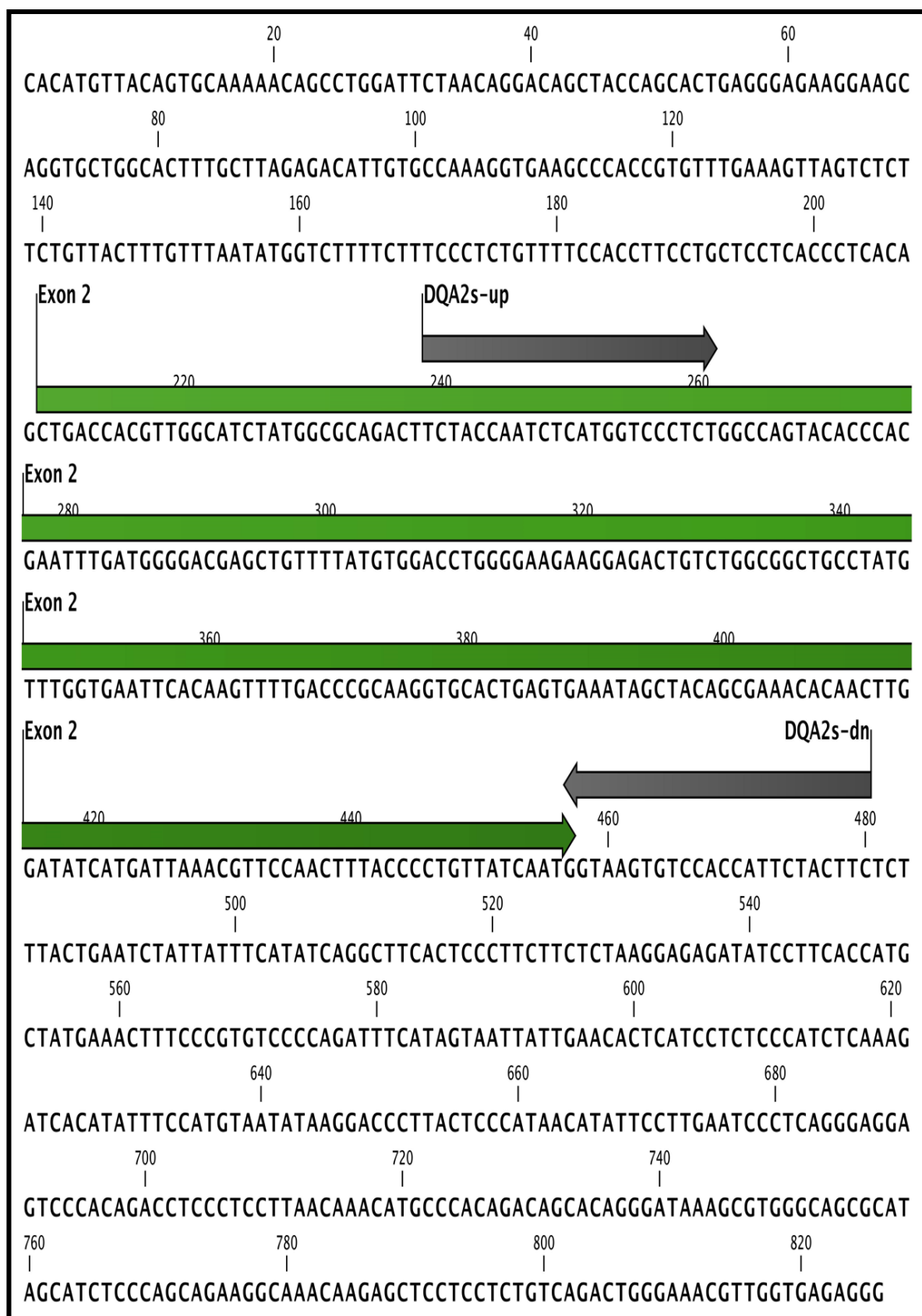


Figure 15 Diagrammatic representation of the second exon of Ovar-DQA2 and immediate flanking region of the Ovar-DQA2 genes showing the location of oligonucleotide primers detailed in Table 27.

5.2.3 Nomenclature

Throughout this chapter, only gene accession number was adopted as the sequences obtained in this study do not cover the whole exon 2. As mentioned earlier in the chapter 2, one of the requirements of inclusion alleles in IPD database (to be registered with IPD name) is to have a complete whole exon 2 sequence.

5.2.4 Phylogenetic Analysis

A compilation of a representative number of sheep, cattle and goat DQA2 (including DQA2-like sequences) was carried out (**Appendix 3**). The GenBank accession numbers of the selected sequences for phylogenetic analysis were: the sheep DQA2 and DQA2-like sequences found in this study (listed in **Table 27**) and from previous studies; AY312376, AY312379, AY312380, AY312383, AY312384, AY312385, AY312391, AY312393, AY312394, AY312395 and AY312396 (Hickford et al. 2004); the cattle DQA2 sequences: D50045, D50454 (Akira et al. 1995), Y07820 (Russell et al. 1997), Y14020-22 (Ballingall et al. 1998), Z48185-93 (Gelhaus et al. 1995) , Z79514-19, Z79522-26 (Ballingall et al. 1997); the goat DQA2 sequences: AY829349-59 (Zhou et al. 2005). The tree was rooted with the human DQA2 sequence NM_020056 (HLA-DQA2*0101, Kenter et al. 1992) as an out group. A neighbour-joining tree (Saitou & Nei, 1987) was constructed on the basis of genetic distances, estimated by the Kimura (1980) two-parameter method, using the MEGA program. GenBank sequences were trimmed to the length corresponding to the PCR amplimers before generating the neighbour-joining tree.

5.3 Results

5.3.1 Sequence Polymorphism of the Second Exon of Ovar-DQA2

A total number of 235 Texel samples were genotyped for Ovar-DQA2. Using DQA2s-up/DQA2s-down amplimers, 241 bp was obtained from the sheep DNA. Under the established conditions, one DQA2-like and eight Ovar-DQA2 sequences were identified from Texel lambs (**Table 28**). All sequences were identical to previously reported sequences.

Table 28 Nomenclature of Ovar-DQA2 and DQA2-like exon 2 alleles detected in Texel

Gene	Accession number	IPD Database Name
DQA2	AY312375	DQA2*0101
	AY312377	DQA2*0103
	AY312381	DQA2*0601
	AY312382	DQA2*0602
	AY312386	DQA2*08012
	AY312387	DQA2*0901
	AY312388	DQA2*1001
	AY312389	DQA2*1101
DQA2-like	AY312392	DQA2*1401

A high degree of variation of nucleotides and amino acids among DQA2 sequences were noticed in Texels; 66 of the 195 nucleotide sites (33.8%) analysed in this study were variable (**Figure 16**). An alignment of the deduced amino acid sequences encoded by exon 2 is shown in **Figure 17**. 39 of the 79 (49.4%) amino acid sites were polymorphic. In general, the variations were clustered into three areas assigned I, II and III (I: 10-15, II: 23-40 and III: 52-85) respectively. The most variation was noticed in amino acid residues $\alpha 10$ (I, S, T), $\alpha 13$ (A, I, T), $\alpha 15$ (F, I, V), $\alpha 52$ (D, G, S), $\alpha 53$ (E, G, Q), $\alpha 55$ (A, S, T), $\alpha 56$ (D, G, S), $\alpha 58$ (D, H, N), $\alpha 65$ (E, N, Q), $\alpha 69$ (A, E, S), $\alpha 71$ (D, H, Q) and $\alpha 79$ (H, R, W) with three different amino acid per sites, and in residues $\alpha 14$ (D, E, H, T), $\alpha 61$ (D, G, R, V), $\alpha 64$ (I, N, R, S), $\alpha 68$ (A, I, K, T) and $\alpha 75$ (I, R, V, Y) with four. The alignment of amino sequences identified dissimilarities of DQA2-like allele, AY312392 from the rest of the alleles, of which the obvious difference was one deleted codon, observed at codon 56. Generally speaking, amino acid variation was found to be common in most of the polymorphic sites based upon previous studies (**Table 29**).

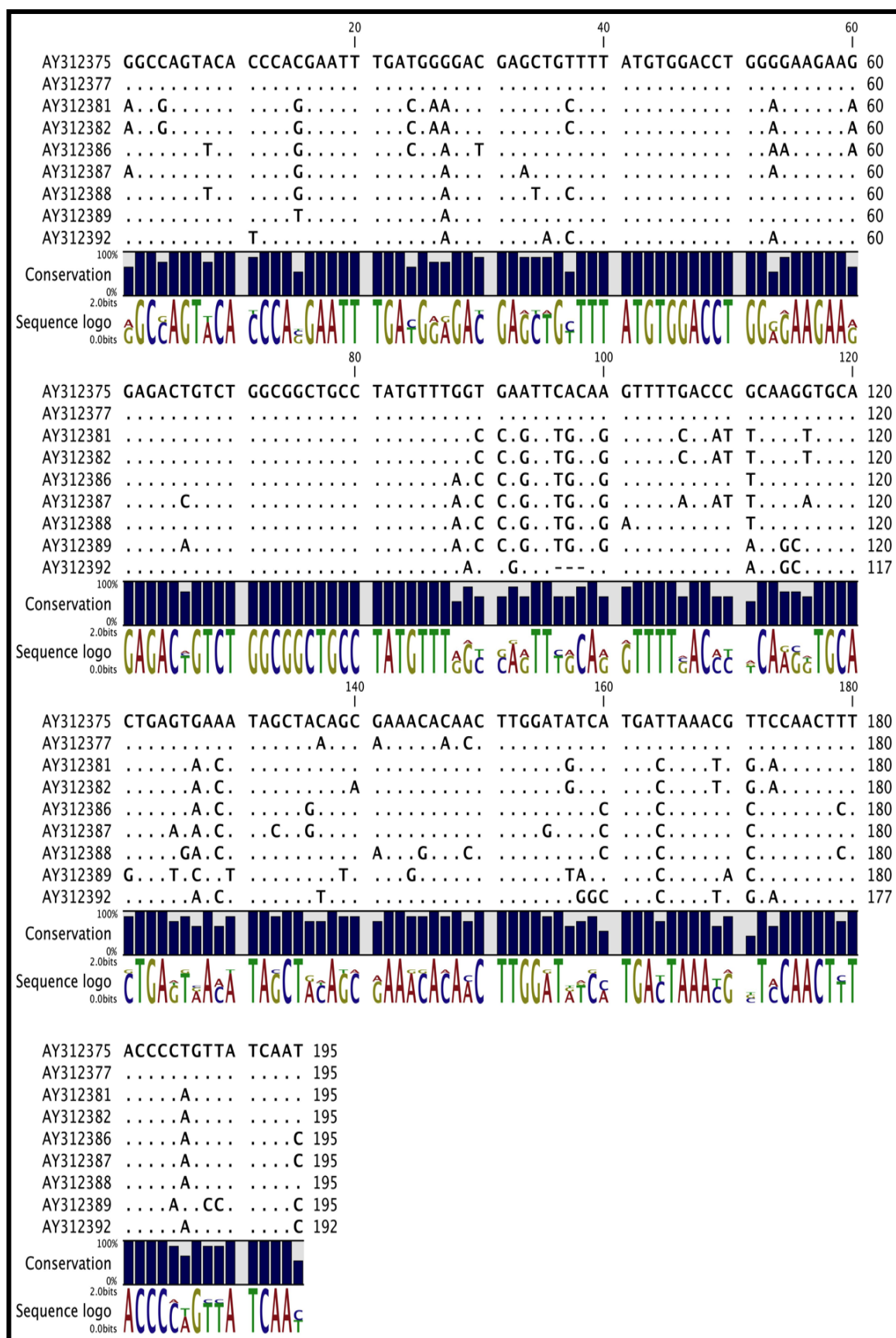


Figure 16 Nucleotide sequences of the second exon of Ovar-DQA2 alleles found in this study. The local allelic nomenclature is used throughout and compared with AY312375. A dot indicates identity with the top sequence

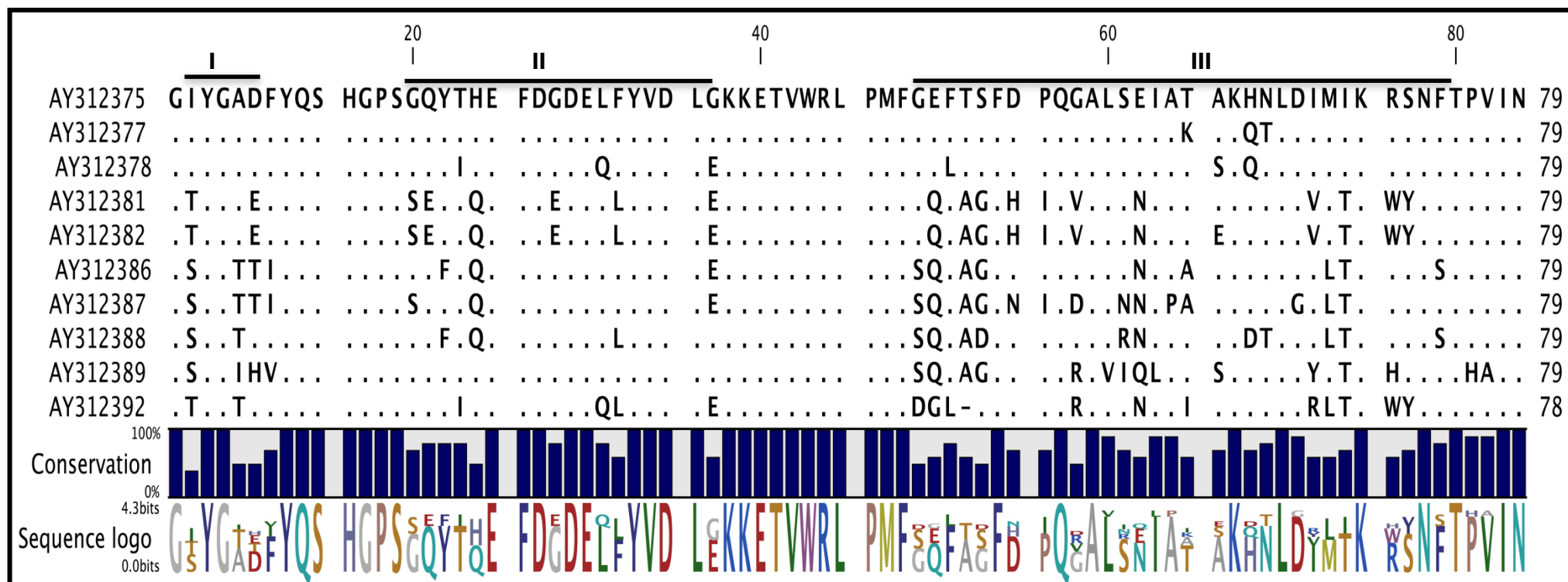


Figure 17 The distribution of polymorphisms within amino acid translations of second exon of DQA2 (including DQA2-like) found in this study. Sequences within polymorphic regions: I, II and III are underlined. A dot indicates identity with the top sequence, AY312375.

Table 29 Amino acid variations in Texel in this study Vs published sheep DQA2 and DQA2-like alleles. Amino acid positions involved in the antigen binding sites (according to Reche & Reinherz, 2003) are indicated by grey background; amino acids that were only found in previous published studies are given in red.

Amino Acid Position	Texel	Previously Published
10	I, S, T	I, C , S, T
13	A, I, T	A, I, T
14	D, E, H, T	D, E, I , H, T, V
15	F, I, V	F, I, V
23	G, S	G
24	E, Q	E, Q
25	F, Y	F, Y
26	I, T	I, T
27	H, Q	H, M , Q
29	F	F, S
31	E, G	E, R
34	L, Q	E , L, Q, R
35	F, L	F, L
40	E, G	E, G
52	D, G, S	D, G, S
53	E, G, Q	E, G, Q
54	F, L	F, L
55	A, S , T	A, I, T, R
56	D, G, S	D, G, R , S
58	D, H, N	D, H, N

59	I, P	I, P
61	D, G, R, V	D, G, R, V
63	L, V	L, V
64	I, N, R, S	I, N, R, S
65	E, N, Q	E, N, Q
66	I, L	I, L
67	A, P	A, P
68	A, I, K, T	A, I, K, T
69	A, E, S	A, E, S
71	D, H, Q	D, H, Q
72	N, T	N, T
74	D, G	D, G, N
75	I, R, Y, V	I, R, Y
76	L, M	L, M
77	I, T	I, T
79	H, R, W	C , H, L , R, W
80	S, Y	S, H , Y
82	F, S	C , F, H
84	H, P	H, P
85	A, V	A, V

5.3.2 Frequencies of the Ovar-DQA2 Alleles

The frequency of each allele in Texel is displayed in **Table 30**. The most frequent DQA2 allele in Texel being AY312375 (23.4%) followed by AY312382 allele (21.1%). One rare allele, namely AY312386 was detected in less than 1% of Texels. The frequency of DQA2-like allele, AY312392 is 23.4% and the frequency of the null allele was 76.6%.

Table 30 Ovar-DQA2 alleles and their frequencies found in Texel

Gene	Allele	Number	Frequency (%)	SE	95 CI (%)	
					Lower	Upper
DQA2	AY312375	110	23.40	1.91	19.57	27.02
	AY312377	96	20.43	1.91	16.81	24.04
	AY312381	64	13.62	1.66	10.43	16.81
	AY312382	100	21.18	1.85	17.87	24.89
	AY312386	4	0.85	0.42	0.21	1.70
	AY312387	41	8.72	1.24	6.17	11.28
	AY312388	31	6.60	1.18	4.26	9.15
	AY312389	24	5.11	1.03	3.19	6.81
DQA2-like	AY312392	110	23.40	1.91	19.79	26.81
	Null	360	76.60	0.91	76.24	80.21

5.3.3 Comparison of Diversity and Frequencies between DQA1 and DQA2

Figure 18 compares allele diversity and frequencies between DQA1 and DQA2. The diversity of DQA1 and DQA2 are similar but their allele frequencies differ. The DQA2 allele frequency distribution is more uniform compared to DQA1.

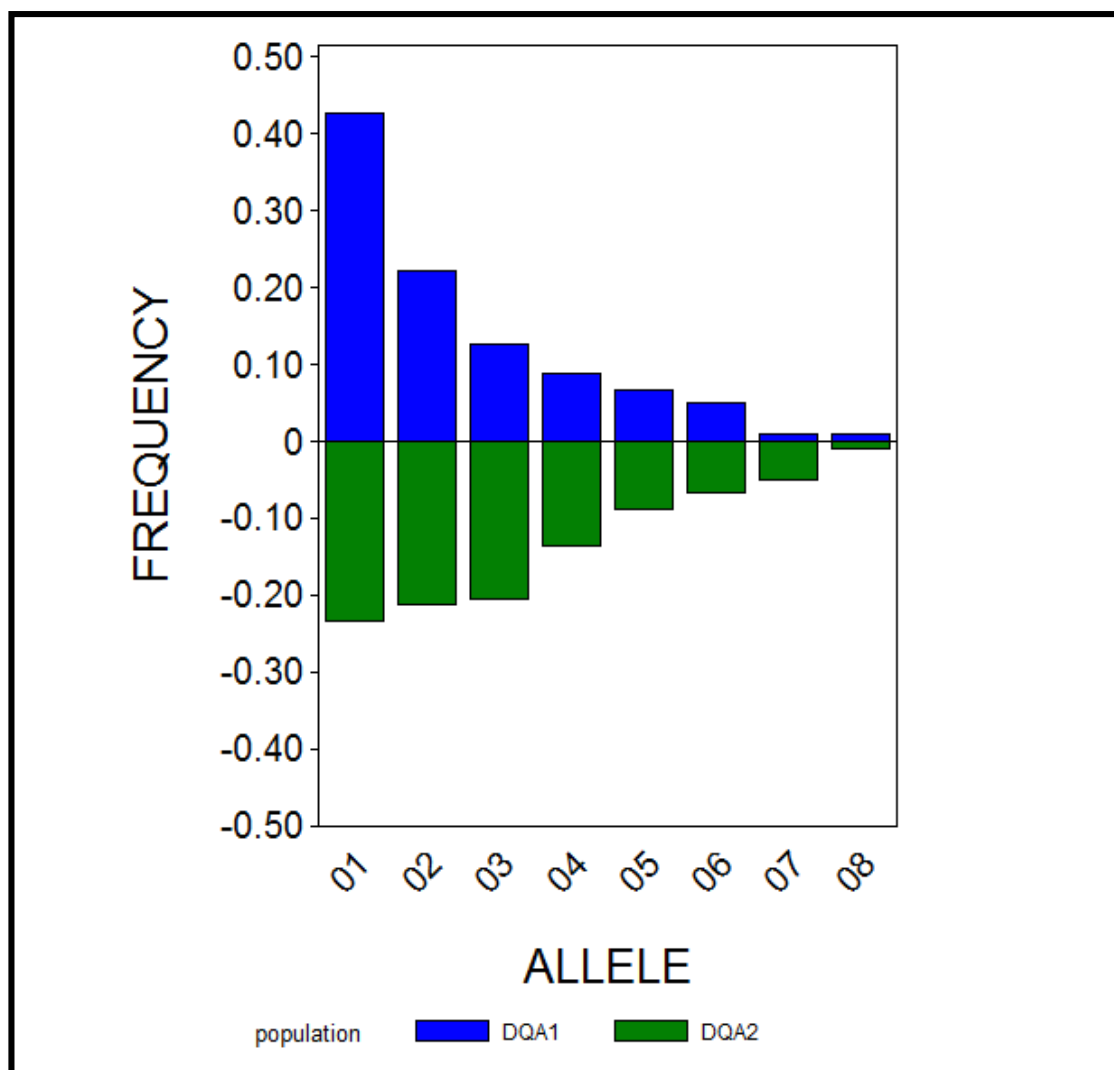


Figure 18 A comparison between diversity and frequencies between DQA1 and DQA2 in Texel

5.3.3 Phylogenetic analysis among of the Ovar-DQA2 Alleles

The phylogenetic tree from DQA2 sequences of this study shows two major separate branches (**Figure 19**). The DQA2-like allele, AY312392 is grouped together with AY312375, AY312377 and AY312389. Five alleles namely AY312381, AY312382, AY312387, AY312386, AY312388 and AY312388 are grouped in a separate cluster.

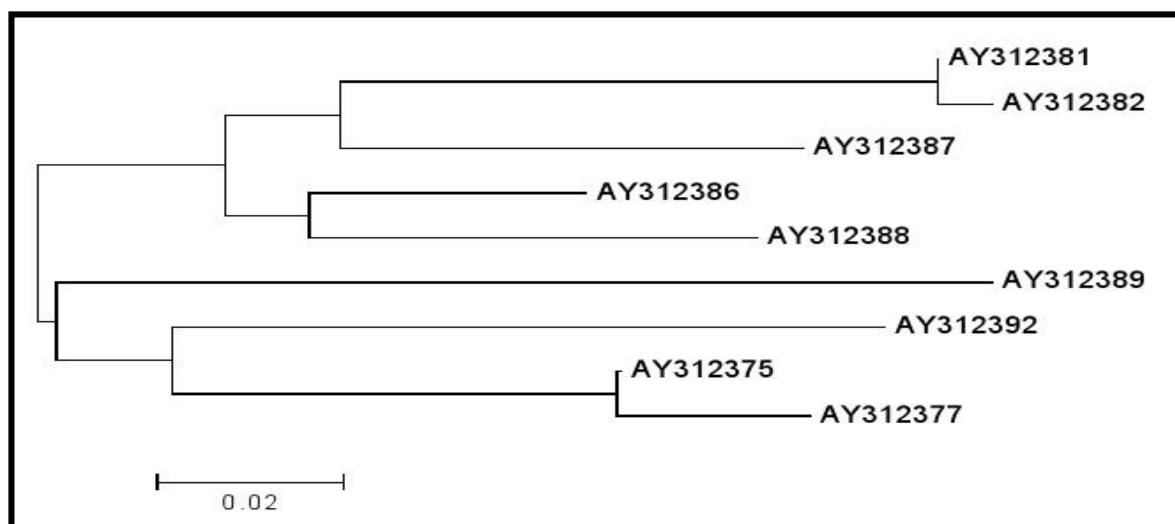


Figure 19 A neighbor-joining phylogenetic tree constructed from exon 2 sequences of DQA2 genes from this study. Branch lengths are proportional to genetic distance.

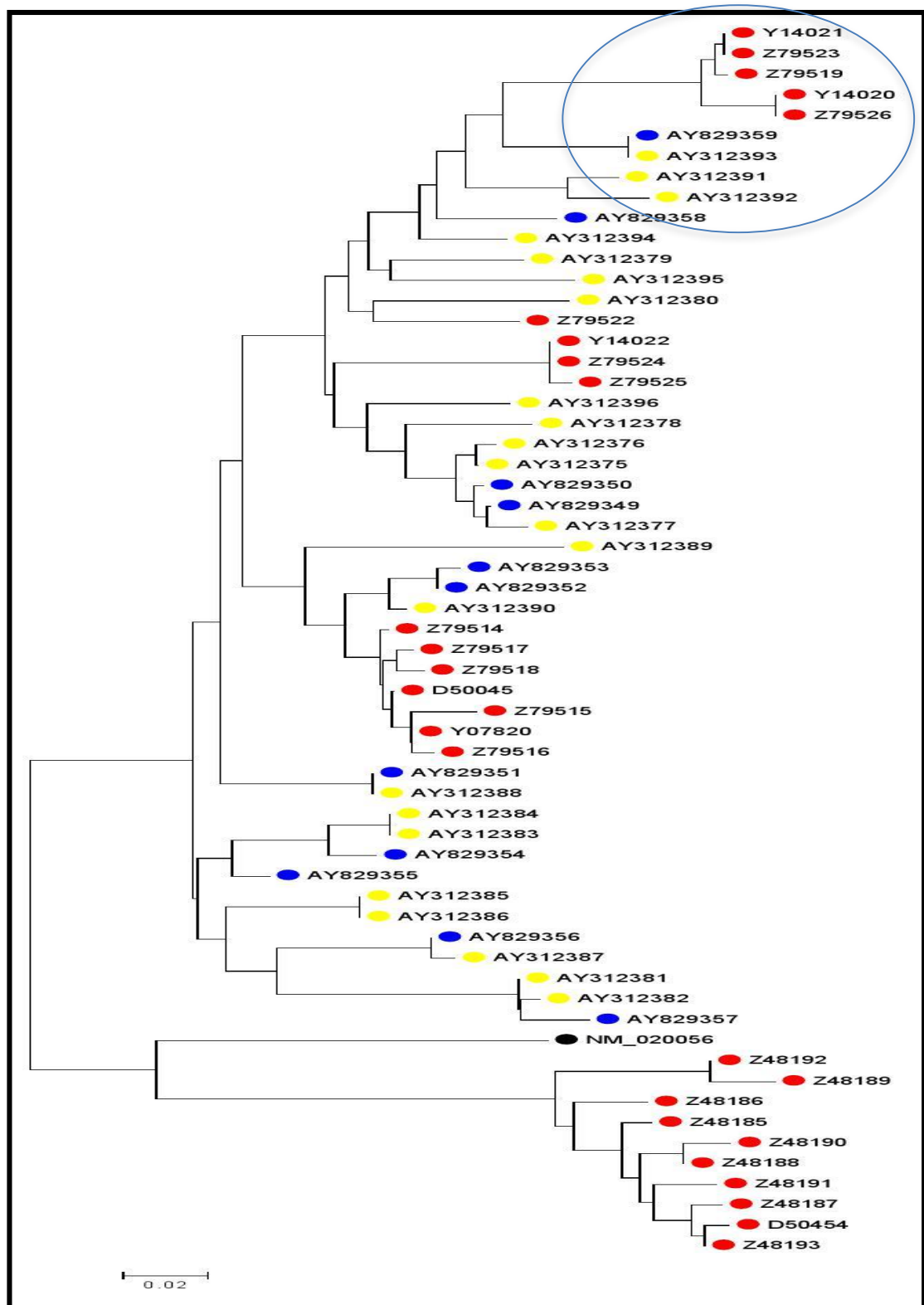


Figure 20 A neighbor phylogenetic tree constructed from exon 2 sequences of DQA2 gene from sheep, cattle and goats. The human DQA2 (NM_020056) was used as an outgroup. Branch lengths are proportional to genetic distance. The yellow, red and blue symbols denote Ovvar-DQA2 (including DQA2-like), BoLA-DQA2 and Cahi-DQA2 respectively.

5.3.4 Haplotype Analysis of the Ovar-DQA

The haplotype of Ovar-DQA was deduced from coinheritance of sequences of sire, dam and lambs (see section 2.5.2). Twelve DQA1-DQA2-DQA2-like haplotypes were identified composed of eight DQA1 alleles (LN827890, LN827891, LN827892, LN827893, LN827894M33304 and Null), eight DQA2 alleles (AY312375, AY312377, AY312381, AY312382, AY312387, AY312388 and AY312389) and two DQA2-like alleles (AY312392 and null). Of these haplotypes, one haplotype, haplotype #i was carrying three DQA genes. A summary of these haplotypes is shown in **Table 31**. AY312392 is only found with two DQA haplotypes; haplotype #i and #l. The rest of the haplotypes were associated with DQA2-like null.

Table 31 DQA Haplotypes found in Texel in this study. The two haplotypes which pose AY312392 allele are shown in bold.

Haplotype	DQA1	DQA2	DQA2-like
#a	LN736359	AY312389	Null
#b	LN827890	AY312388	Null
#c	LN827890	AY312387	Null
#d	LN827891	AY312382	Null
#e	LN827892	AY312381	Null
#f	LN827893	AY312386	Null
#g	LN827894	AY312381	Null
#h	M33304	AY312375	Null
#i	M33304	AY312375	AY312392
#j	M33304	AY312377	Null
#k	M33304	AY312382	Null
#l	Null	AY312375	AY312392

5.4 Discussion

This is the first report on the variation of DQA2 and DQA2-like loci in Texel sheep, using sequence-based typing. Sequencing of the exon 2 DQA2 DNA in this study revealed 197 bp nucleotides encoding a protein of 79 amino acids. Sequence analyses revealed eight DQA2 and one DQA2-like genes, with no new alleles reported in this study. Insertion or deletion from one DQA2-like nucleotide sequence was observed and twelve haplotypes of DQA were identified in this Texel flock. DQA haplotype analysis suggests that some sheep have three genes per haplotype.

Previously, RFLP and SSCP were being used for typing DQA2 (Hickford et al. 2004; Ennen et al. 2005; Ballingall et al. 2015), however, in this study, we have developed the sequence-based typing system for Ovar-DQA2. Haplotype checking was used as a precaution to detect any errors in assigning alleles. It was noticed that one primer pair is sufficient for amplification of DQA2 system in this flock. However, typing with another set of primers which is located in introns could be used in the future in order to amplify the whole exon 2 region. The peptide binding region is located exon 2 of α chain, thus the whole exon 2 sequences gives additional information on the peptide binding region. In addition, the use of an additional primer could also validate amplified allele assignments from the other primers (Ballingall & Tassi 2010).

The variation of DQA2 has been demonstrated in this Texel flock. In total, eight DQA2 and one DQA2-like alleles have been determined. This result confirms the earlier result that DQA2 in sheep is polymorphic (Escayg et al. 1996; Snibson et al. 1998; Hickford et al. 2004; Ennen et al. 2009; Gelasakis et al. 2013). No novel sequences were detected in this study and all sequences were similar to previously described alleles (Hickford et al. 2004).

This study also confirms the presence of DQA2-like alleles, as shown in Hickford et al. (2004). DQA2-like alleles were thought to result from ancient recombination between DQA1 and DQA2 loci (Ballingall et al. 2015). Interestingly, only one DQA2-like allele, AY312392 or *1401 was found in this Texel flock. Uniquely, this allele has a three nucleotides deletion or one codon, supporting the idea that the DQA2-like protein is different than DQA2 (Ballingall et al. 2015). Hickford et al. (2004) asserted that *1401 allele is an important allele which is preserved by natural selection. Furthermore, the

fact that DQA2-like loci predate Bovidae speciation (Ballingall et al. 2015) shows the importance of the allele in vital functions.

DQA haplotype analysis in this breed has shown that some sheep have three DQA genes per haplotype. This contradicts the earlier analyses that the DQA haplotype possesses only two genes (Hickford et al. 2007; Ballingall et al. 2015). The presence of a DQA2-like allele is associated with the absence of DQA1 allele, thus maintaining two genes per haplotype (Hickford et al. 2007; Ballingall et al. 2015). The finding of this study affirms the existence of a DQA3 locus in sheep, as seen in cattle (Ballingall et al. 1997). The failure to detect a DQA3 locus in previous studies could be a consequence of the different technique used or DQA haplotype number which varies between sheep. The inter-haplotype pairing of DQA and DQB molecules forms functional restriction elements in cattle (Glass et al. 2000). Further characterization with DQB genes may elucidate the reason.

The sequence of Texel DQA2 exhibits variation. Out of the 79 amino acids found in Texel, almost half (49%) were polymorphic. The most polymorphic sites were observed at three sites (α 14, α 61 and α 68) which are included in the putative antigen-binding region. It is possible that specific amino acids in this region play a fundamental role in protection against certain diseases. The DQA2 and DQA2-like genes have been associated with resistance against ovine footrot in Merino and Chios sheep populations (Ennen et al. 2009; Gelasakis et al. 2013).

We noticed the allele frequency of DQA2 in Texel differed from other breeds. The most prevalent allele in this study is AY312375 or DQA2*0101. The work of Gelasakis et al.(2013) found that DQA2*0301 was common in alleles in the Chios breed, but not detected in this study. Differences in DQA2 allelic distribution among the sheep breeds was noted, as demonstrated previously (Hickford et al. 2004).

5.5 Conclusion

High diversity of the Ovar-DQA2 gene has been detected in the Texel. This study provides evidence that the Texel DQA haplotype is composed of 3 DQA genes in some sheep. Sequence-based typing is an efficient tool for typing DQA2 in sheep.

CHAPTER 6

GENETIC DIVERSITY OF OVAR-DQB1 IN TEXEL

6.0 Summary

MHC diversity is associated with economically important diseases in livestock. In this chapter, Ovar-DQB1 gene diversity in a Texel population was determined through sequence-based typing. A total of 13 Ovar-DQB1 alleles were identified. The alignment of these alleles revealed the existence of 33 amino acid polymorphic sites, four of which had three substitutions per site: residues $\beta 13$ (I, K, M), $\beta 32$ (F, I, L), $\beta 39$ (A, L, V) and $\beta 87$ (D, E, Y), and five had four substitutions per site: residues $\beta 10$ (F, H, V, Y), $\beta 15$ (H, L, Q, R), $\beta 27$ (H, L, S, Y), $\beta 38$ (D, F, H, Y) and $\beta 58$ (D, H, S, Q). The most prevalent DQB1 allele was GU191455 (together with GU19159) with a frequency of 26.2% in this population. Some of Ovar-DQB1 sequences are on the same main branch of the phylogenetic tree as goat DQB1 as compared to some sheep DQB1. In this work, sequence-based typing was applied to capture DQB1 diversity in sheep. High amounts of diversity of DQB1 locus were found in this population.

6.1 Introduction

A major impetus for research on the MHC genes in livestock is the hope of finding relationships between MHC polymorphism and economically important diseases. The degree of polymorphism of MHC genes is displayed through three levels: (i) a high number of alleles (ii) the presence of multi gene loci (iii) high variation of nucleotide variation between any two alleles. The Ovar-MHC has been consistently associated with nematode and footrot resistance (Schwaiger et al. 1995; Dukkupati et al. 2006a, b).

In sheep, the presence of class II loci which are homologous to HLA-DQB was confirmed by Chardon et al. (1985). There are two loci, DQB1 and DQB2, which are both transcribed (Wright & Ballingall, 1994). The nucleotide sequences obtained from Ovar-DQB1 and Ovar-DQB2 are similar with >90% similarity reported (Wright & Ballingall, 1994). Previous work using reference-strand-mediated conformation analysis (RSCA) has demonstrated the diversity and polymorphism of exon 2 DQB sequences in Blackface and Merino sheep (Feichtlbauer-Huber et al. 2000). A genomic study of Rambouillet sheep shows DQB1 containing five exons (Herrmann-Hoesing et al. 2008). Among these five exons, exon 2 is of interest because it encodes the peptide binding region (Scott et al. 1991a).

High polymorphism presents a serious challenge to the development of reliable genotyping methods. It is important to find a reliable typing method that can cope with large numbers of alleles. Sequence-based typing is used in ruminants to type MHC loci, namely in cattle (Takeshima et al. 2007) and sheep (Ballingall et al. 2008; Ballingall & Tassi, 2010). This typing provides a significant advantage over other commonly used typing techniques because it is rapid, able to differentiate between highly similar alleles and to capture all polymorphic sites and amplify all alleles (Stear et al. 2007). However, to date its application in sheep is still rare. To our knowledge, so far only has been performed in one locus, DRB1 (Sayers et al. 2005b; Ballingall et al. 2008; Ballingall & Tassi, 2010). What is still not reported is the diversity DQB1 in Texel population. In an attempt to answer this question, sequence-based typing was used. In addition, the evolutionary relationship between DQB1 alleles was also investigated.

6.2 Materials and Methods

6.2.1 Primers

The JM05/JM06 and 991/994 primer pairs were used in this study (**Table 32**) and **Figure 21** displays the primer-binding region. As illustrated in the **Figure 21**, the primer pair of JM05/JM06 was positioned in the flanking region of the exon 2, and the second primer pair was located within intron 1 and intron 2. The JM05/JM06 were designed based on the OLA-DQB*1 sequence (Scott et al. 1991a). The latter primers, 991/994 were designed in order to obtain complete exon 2 DQB1 and validate the results obtained from the JM05/06 primer.

6.2.2 Amplification and Sequencing of Ovar-DQB1

The PCR reaction used and the band sizes amplified by JM05/JM06 and 991/994 are shown in **Table 32**. For JM05/JM06, the reaction was performed under the following conditions; one cycle of incubation for 94°C for 7 min, followed by 33 cycles of 94°C for 30 s, 60°C for 30 s and 72°C for 45 s. On the other hand, touch-down amplification was performed for 991/994, with an initial step of 95°C for 15 min, followed by 7 cycles of 95°C for 30s, annealing temperatures starting at 66°C for 45s (decreasing by 0.5°C/cycle), and 74°C for 45 s for extension. This step was followed by 30 cycles of 95°C for 30 s, 63°C for 45s and 74°C for 45 s. As described in Chapter 2, a novel allele was cloned into the pGEM-T-easy vector.

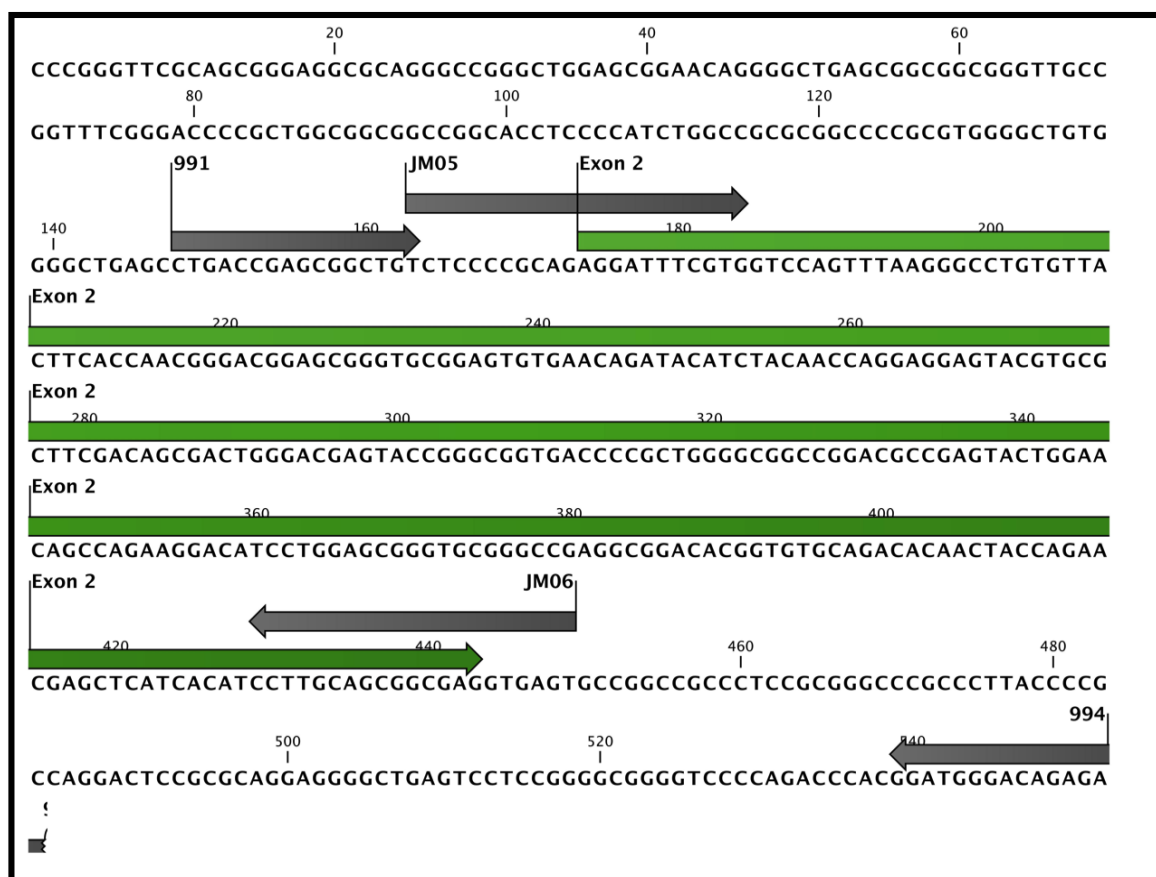


Figure 21 Diagrammatic representation of the second exon of Ovar-DQB1 (Z28424 sequence) and immediate flanking region of the Ovar-DQB1 genes showing the location of oligonucleotide primers detailed in Table 32.

Table 32 PCR primers used for the amplification of the second exon of Ovar-DQB1 gene in this study

Primer Name	Primer Location*	Primer Sequence	Amplicons size (bp)	Number of Cycles	Reaction conditions
JM05	195-214	TCT CCC CGC AGA GGA TTT CGT G	278	33	94°C for 7 min, then 94°C for 30s, 60°C for 30 s, 72°C for 45s
JM06	453-473	CTC GCC GCT GCC AGG TGA AGG			
991	178-193	CTG ACC GAG CGG CTG T	405	7 (phase1) + 30 (phase 2)	95°C for 15 min, then phase 1 (95°C for 30s, 66°C-0.5°C/cycle for 45s, then phase 2 (95°C for 30s, 63°C for 45s, 74°C for 45s)
994	566-583	CGG CTC TCT GTC CCA TCC			

* The primer position refers to Ovar-DQB1 sequence Z28424 reported in Ballingall et al. (1994).

6.2.3 Nomenclature

Throughout this chapter, the gene accession number was adopted.

6.2.4 Phylogenetic Analysis

A compilation of a representative number of sheep, cattle and goat DQB1 sequences was carried out (**Appendix 3**). Two phylogenetic trees were constructed. The first phylogenetic tree comprises of all sequences from sheep DQB1 extracted from this study (**Table 33**). The second phylogenetic analysis used the sheep DQB1 found in this study, the cattle DQB1 sequences: U77786-94 (Sigurdardottir et al. 1992) and the goat DQB1 sequences: AY464658 and AY464659 (Amills et al. 2004). The tree was subsequently rooted with the human DQB1 sequence HLA-DQB1*0101 (AF217417; Donner et al. 2000) as an out group. A neighbour-joining tree (Saitou & Nei 1987) was constructed on the basis of genetic distances, estimated by the Kimura (1980) two-parameter method, using the MEGA program. GenBank sequences were trimmed to the length corresponding to the PCR amplicon JM05/JM06 before generating the neighbour-joining tree.

6.3 Results

6.3.1 Sequence Polymorphism of the Second Exon of Ovar-DQB1

A total of 235 Texel DNA samples were genotyped for Ovar-DQB1 using the first primer set, JM05/JM06. Using these amplimers, 278 bp were obtained from the sheep DNA. A total of 13 different Ovar-DQB1 sequences, including null were identified (**Table 33**). Two of them were new sequences, and have not been previously reported. These sequences were submitted to EBI database with accession numbers LN811403 and LN811404. Three different sequences were obtained from over 20% of sheep using the JM05/JM06 primers; alleles GU191455 and GU191459 alleles were amplified together with other alleles.

Table 33 Nomenclature of Ovar-DQB1 exon 2 alleles detected in this Texel population

Local name	Accession number
AH001247	AH001247
DQB*21	AJ238939
DQB*27	AJ238945
New1	GU191453
Tnew1	GU191455
Tnew3	GU191456
Tnew4	GU191457
13a	GU191460
new2	HQ728667
8t040	LN811403
9t027	LN811404
Z28423	Z28423

While using the second set of primers, 991/994, 405 bp were obtained. The sequences covered the whole exon 2. Six new alleles; LN868258 LN868259, LN86261, LN868262, LN868263 and LN868264 were isolated. With this second set of primer, only GU191455 allele (without GU191459) sequence was found.

In this chapter, the nucleotide and amino acid variations obtained from the first set of primers, JM05/JM06 were analysed. The reason being all Texel DNA samples used were analysed with this first primer set. There were considerable nucleotide and deduced amino acid variation between 13 DQB1 found in this Texel population. Out of the 238 nucleotide sites, 51 (21.4%) were polymorphic as shown in **Figure 22**. 33 (41.7%) of the amino acid polymorphic were identified (**Figure 23**). Most variation was found in amino acid residues β 13 (I, K, M), β 32 (F, I, L), β 39 (A, L, V) and β 87 (D, E, Y) with three different amino acid per sites, and in residues β 10 (F, H, V, Y), β 15 (L, H, Q, R), β 27 (L, H, S, Y), β 38 (D, F, H, Y) and β 58 (D, H, Q, S) with four (**Table 34**).

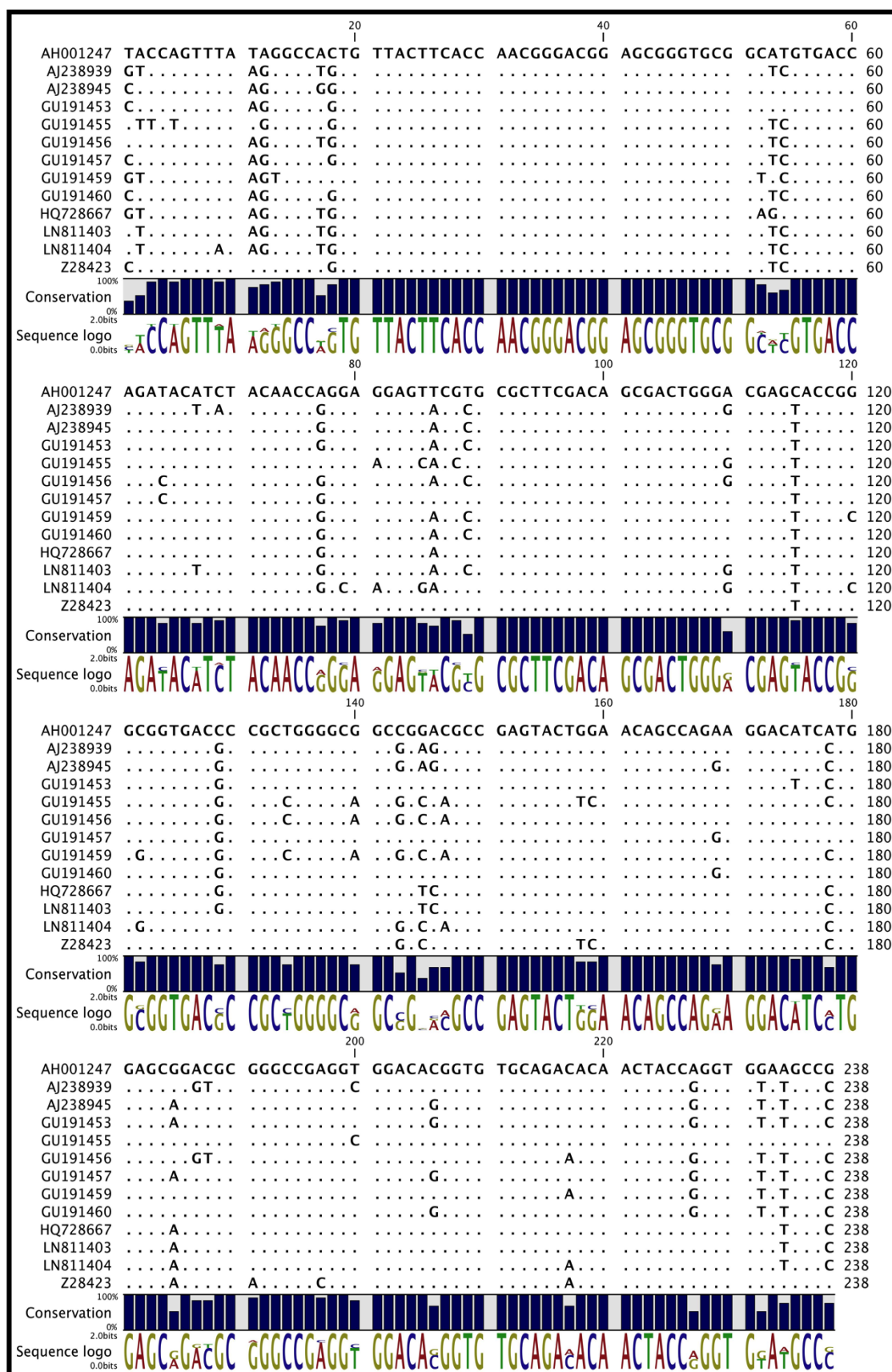


Figure 22 Nucleotide sequence of the second exon of Ovar-DQB1 alleles found in this study

Table 34 Amino acid variation in Texel sheep in this study. Amino acid positions involved in the antigen binding sites (according to Reche & Reinherz,2003) are indicated by grey background.

Amino Acid Position	Texel in this study
10	F, H, V, Y
11	L, Q
12	F, L
13	I, K, M
14	C, G
15	H, L, Q, R
27	H, L, S, Y
31	H, Y
32	F, I, L
35	Q, R
36	E, Q
38	D, F, H, Y
39	A, L, V
45	D, G
56	Q, R
57	P, R
58	D, H, Q, S
62	F, W
66	E, K
68	F, I
69	L, M
71	Q, R
72	T, V
73	Q, R
75	A, E
76	A, V
78	T, R
82	H, N
85	Q, R
87	D, E, Y

6.3.2 Frequencies of the Ovar-DQB1 Alleles

The frequency of each DQB1 allele in Texel is shown in **Table 35**. The most frequent DQB1 allele in Texel is GU191455 (together with GU19159) (22.6%), followed by null (20.4%). Three rare alleles, namely GU191453, GU191457 and LN811403 were detected which contributed less than 1% in Texel.

Table 35 Ovar-DQB1 and their frequencies found in Texel in this study

Allele	Number	Frequency (%)	SE	95 CI (%)	
				Lower	Upper
AH001247	20	4.26	1.00	2.34	6.38
AJ238939	31	6.60	1.18	4.26	9.15
AJ238945	24	5.11	1.03	3.19	6.81
GU191453	2	0.43	0.30	0.00	1.06
GU191455 (GU191459)	106	22.55	1.88	19.15	26.17
GU191456	59	12.55	1.62	9.36	15.74
GU191457	2	0.43	0.30	0.00	1.06
GU191460	37	7.87	1.19	5.53	10.43
HQ728667	76	16.17	1.72	12.98	19.36
LN811403	4	0.85	0.42	0.21	1.70
LN811404	8	1.70	0.59	0.64	2.77
Null	96	20.43	1.76	17.02	23.62
Z28423	5	1.06	0.47	0.21	2.13

6.3.3 Phylogenetic analysis among of the Ovar-DQB1 Alleles

A phylogenetic tree was constructed from exon 2 of the Ovar-DQB1 sequences. One of new sheep DQB1 alleles, LN811403 sequence was clustered together with previously reported alleles, HQ728667, whereas the other new allele, LN811404 was separated in other clusters (**Figure 24**). The GU191459 was clustered together with AH001247 and Z28423.

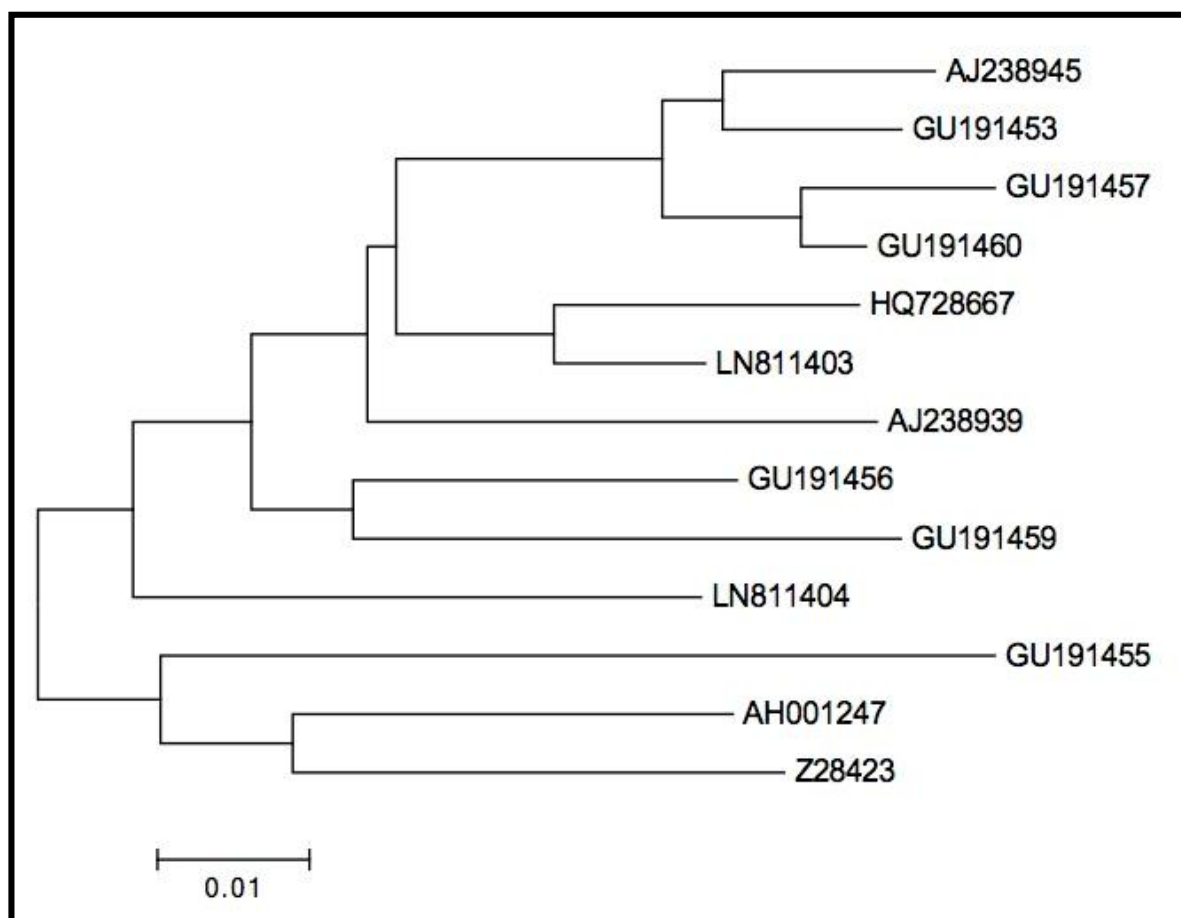


Figure 24 A neighbor phylogenetic tree constructed from exon 2 sequences of DQB1 gene from this study length are proportional to genetic distance.

A phylogenetic tree was also constructed from DQB1 sequences obtained from this study together with the reported cattle and goat DQB1 sequences. It revealed three main clusters. Some sheep DQB1 alleles cluster with goats DQB1 to make-up cluster I. The cattle and sheep DQB1 formed separate clusters observed in the clusters II and III respectively (Figure 25).

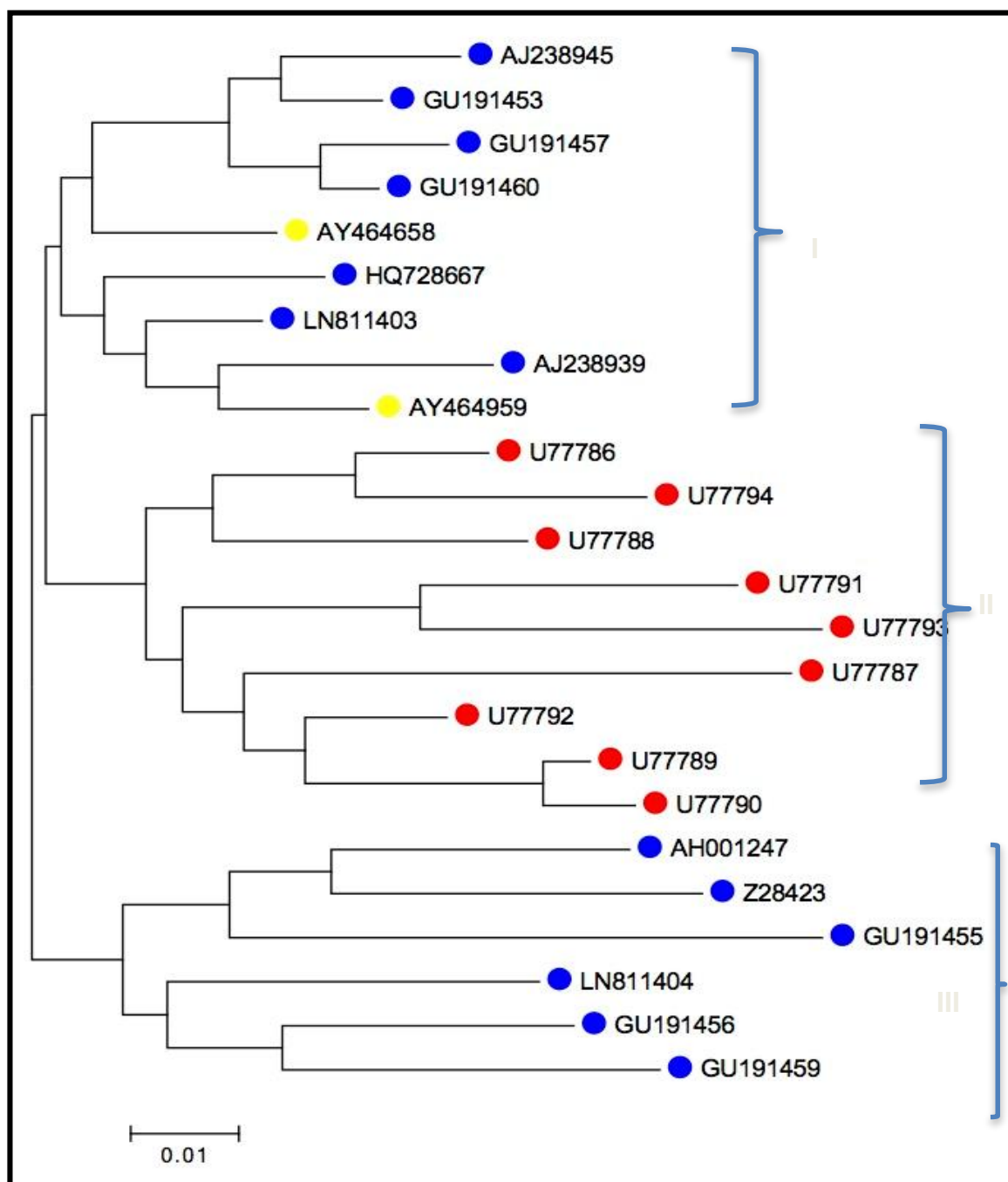


Figure 25 A neighbor phylogenetic tree constructed from exon 2 sequences of DQB1 gene from sheep, cattle and goats branch lengths are proportional to genetic distance. The blue, red and yellow symbols denote Ovar-DQB1, BoLa-DQB1 and CahI-DQB1 respectively.

6.4 Discussion

Sequence-based typing was used and revealed 238bp nucleotides encoding 79 amino acids at the second exon of DQB1. From this population, 13 DQB1 alleles were identified. The alignment of nucleotide and amino acid of this sequence revealed high polymorphism. The most common DQB1 allele is GU191455 (together with GU191459), followed by null. Phylogenetic analysis indicated some DQB1 alleles have closer relationship with goat DQB1 compared to sheep DQB1.

Sequence-based typing is a reliable, robust yet simple typing method for MHC genes (Ballingall et al. 2008). However, the primer design for specific population is challenging. Two sets of primers; JM05/JM06 and 991/994 were used to amplify Ovar-DQB1 alleles in this study. The first set of primers, JM05/JM06 succeeded to amplify DQB1 alleles. Two new alleles were found and subsequently submitted to the database. However, more than two DQB1 sequences were obtained from single sheep with this primer set. This appears to be exclusively for combination of GU191455/GU191459 and one other allele. Interestingly, GU191459 was reported as one of the DQB2 alleles, suggesting that the JM05/JM06 primer set, not only amplifies DQB1 gene but also the DQB2. This contradicts the hypothesis that JM05/JM06 is a locus specific primer for DQB1 based on the 3 prime end of exon 2 (van Oorschot et al. 1994).

The second primer which was located in conserved region of introns 1 and 2 was designed for two purposes. The first primer set does not amplify the whole exon 2 sequence. Secondly, the use of an other set of primers also can validate the result obtained from the first primer (Ballingall & Tassi 2010). The second set of primers covers a longer nucleotide sequence, thus the extended sequences were submitted to the database as new alleles. A total of six new alleles were identified from this set of primers. Unlike the first set of primers, amplification of more than two DQB1 sequences did not occur with the second set of primers. This result suggests that the 991/994 primer set is a better primer than the JM05/JM06 for detection of DQB1 in sheep. Nevertheless, this claim needs to be carefully considered, as the 991/994 primer set has not been used for detection of all alleles in this study.

This study has characterized the diversity of DQB1 in a Texel population. 13 DQB1 alleles were detected from 235 Texel DNA samples. This finding confirms that DQB1 is

a highly polymorphic locus, like other MHC class II loci. It also confirms that DQB1 is more polymorphic than DQA1 and DQA2 in this population. The sequence of DQB1 exhibits variation including an area which is an important peptide binding site, and showing the similar pattern in goat (Amills et al. 2004). Our results provide further evidence of polymorphisms of DQB being conserved in ruminants (Amills et al. 2004). This conservation site is most likely due to its role in presenting antigen to T cells (Amills et al. 2004).

A high frequency of null alleles (20%) was observed this study. This is most likely due to the fact that the DQB1 null is associated with the presence of other locus, similar observations with DQA1, in which DQA1 null is associated with presence of DQA2-like (Hickford et al. 2007). The presence of high frequency of null at DQB1 loci suggests that this locus may not be important for antigen presentation. However, this inference contradicts the experimental study of Hui et al. (2012) who suggest that DQB1 gene are important gene for encoding MHC molecules. In addition, the possibility of nucleotide polymorphism in the primer binding sites occurred which can result in prevention of amplification of PCR product cannot be ruled out.

The population tree revealed clear topologies, which showed some of the sheep DQB1 alleles having a close relationship with goat DQB1 and cattle DQB1. These clusters of two ruminant species support the trans-species hypothesis (Klein 1987), in which ancient sequences that are present in a common ancestor have been retained in several species since their divergence. These alleles maybe important in facing common pathogens in the environment.

6.5 Conclusion

In conclusion, DQB1 is a polymorphic locus in Texel population. Sequence-based typing for sheep DQB1 has been developed in this study. The optimum primer design is fundamental aspect in sequence-based typing in achieving accurate MHC typing in populations.

CHAPTER 7

GENETIC DIVERSITY OF OVAR-DQB2 IN TEXEL

7.0 Summary

The MHC class II molecules are membrane-integrated glycoproteins which appear as heterodimers; alpha and beta chains on the surface of antigen presenting cells. They are involved in antigen presentation to T cells, leading to the induction of protective immunity. Polymorphism in the alpha and beta chain determines the peptide binding specificity, hence typing of this polymorphism is of great interest. However this gene, DQB2, is not widely reported in sheep. In this chapter, Texel DQB2 diversity was investigated by sequence-based typing. A total of 16 different DQB2 alleles were identified. The alignment of these alleles in Texel sheep revealed the existence of 32 amino acid polymorphic sites, seven of which β 14 (H, L, Q), β 28 (K, N, T), β 30 (N, Q, Y), β 38 (A, L, V), β 45 (D, G, N), β 47 (F, H, Y), β 56 (P, Q, R) have three amino acid substitutions. Four amino acid substitutions were found at the three amino acid sites (β 9, β 26, β 37). Five amino acid substitutions were observed in residues β 57 (D, E, H, Q, S) and β 85 (A, G, L, N, V). The diversity of Texel DQB2 was reported in this work. The potential of sequence-based typing of Ovar-DQB2 was also discussed.

7.1 Introduction

The MHC is a special genomic region for vertebrates because it contains genes crucial in adaptive immune response. MHC class II genes encoding cell surface molecules, known as MHC molecules, function to present antigens to T cells. MHC class II molecules consist of two proteins, an alpha and beta, which are encoded by separate MHC loci.

In sheep, the detail of genomic organisation of MHC class IIa region has been reported by Herrmann-Hoesing and co-workers (2008). They have determined that the MHC class IIa consist of DRB, DQA and DQB. The DQB loci are polymorphic (Scott et al. 1991; Fabb et al. 1993; Wright & Ballingall, 1994) and divided into DQB1 and DQB2 (Herrmann-Hoesing et al. 2008).

Like other MHC class II loci, the most interesting region is exon 2 of those loci, of which some of the polymorphisms in this region determine peptide binding specificity. Although much effort has been devoted to the study of polymorphisms in exon 2 of DRB1, the polymorphism of the same region of DQB2 still remains unclear. In addition, there is a paucity of information on the variation of DQB in sheep (Feichtlbauer-Huber et al. 2000). The aim of this chapter is to describe the diversity of DQB2 found by sequence-based typing in the Texel population. In addition, distributions of allele frequencies and evolutionary relationships between DQB alleles shall be described.

7.2 Materials and Methods

7.2.1 DNA Source

See 3.2.1.

7.2.2 Primers

The JM05/JM07, 1005/1007 and MJS05/JM07 primer pairs were used in this study (**Table 36**) and **Figure 26** identifies the primer-binding region. The JM05/JM07 was designed based on OLA-DQB*2 sequence (van Oorschot et al. 1994). As illustrated in **Figure 26**, the primer pair of JM05/JM07 is in the flanking region of exon 2.

By use of the first primer, most of DQB2 alleles were identified except AJ2389435 and AJ238946 which was not well amplified in some heterozygote samples. This was detected through haplotype analysis. Thus, the second set of primers, 1005/1007, was designed for the amplification of those two alleles. The primers 1005 and 1007 were located within intron 1 and intron 2 respectively (to amplify the whole exon 2). However, it amplified a non MHC sequence (pericentrosomal, U62384). Later, the third primer set, MJS05/JM07 was designed for purpose of detecting those two alleles.

Table 36 PCR primers for the amplification of the second exon of Ovar-DQB2 gene

Primer Name	Primer Location*	Primer Sequence	Amplicons size (bp)	Number of Cycles	Reaction conditions
JM05	163-184	TCT CCC CGCAGAGGATTTTCGTG	277	33	94°C for 7 min, then 95°C for 30s, 65°C for 30s and 72°C for 45s
JM07	419-440	GCCGCTGCAAGGAGGTGATGA G			
1005	148-165	CTG ACC GAG CGG CTG TCT	403	7 (phase1)	95°C for 15 min, then phase 1 (95°C for 30s , 66°C-0.5°C/cyclefor 45s), then phase 2 (95°C for 30s, 63°C for 45s and 74°C for 45s)
1007	488-502	CTC GCG CGC TGA GTC		+ 30 (phase 2)	
MJS05	163-184	TCC CCG CAG AGG ATT TCC TG	277	33	94°C for 7 min, then 95°C for 30 s, 65°C for 30 s, 72°C for 45s
JM07	419-440	TCCGCTGCAAGGAGGTGATG			

*The primer position refer to Z28424 reported in Ballingall et al. 1994

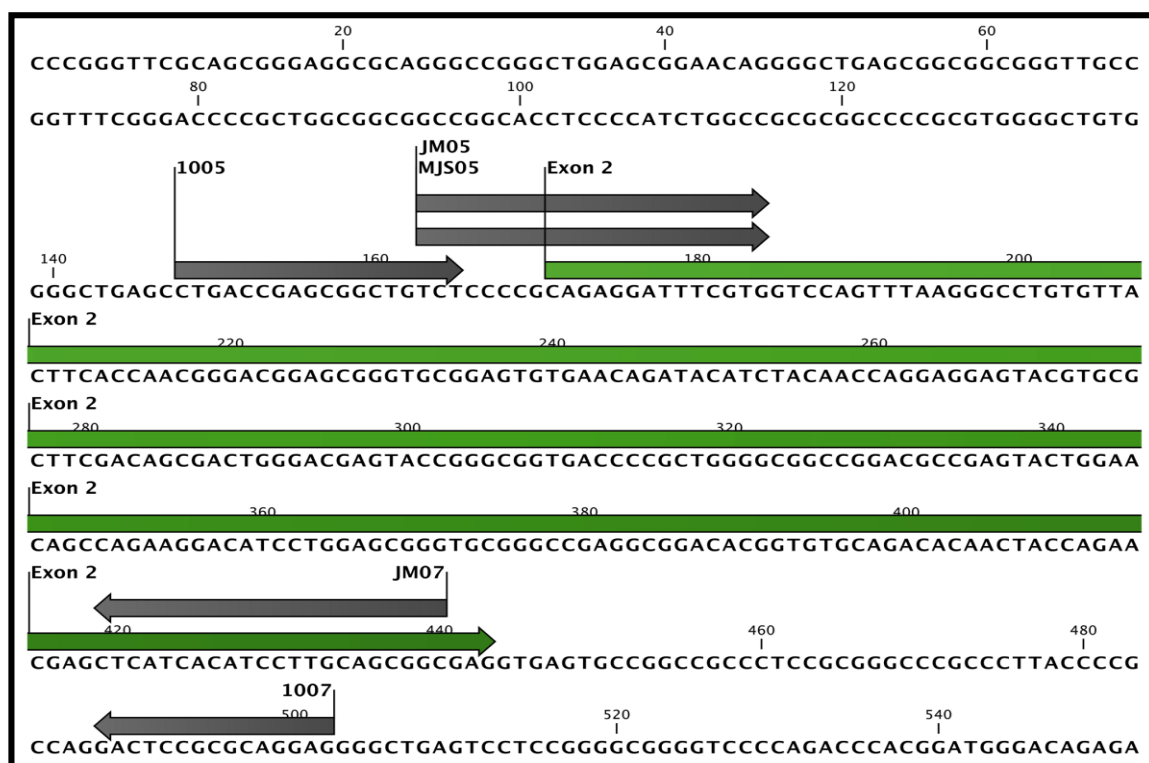


Figure 26 Diagrammatic representation of the second exon of Ovar-DQB2 and immediate flanking region of the Ovar-DQB2 genes showing the location of oligonucleotide primers detailed in Table 36.

7.2.3 Amplification and Sequencing of Ovar-DQB2

For the PCR reaction, 1µl of the DNA containing solution was added to 20µl of the PCR master mix as described in **Chapter 2**. The PCR reactions used and the band sizes amplified by JM05/JM07, 1005/1007 and MJS05/JM07 are shown in **Table 37**. For JM05/07 and 1005/1007 primer pairs, reaction was performed under the following conditions; one cycle of incubation for 94°C for 7 min, followed by 33 cycles of 95°C for 30s, 65°C for 30s and 72°C for 45s. For 1005/1007 pair, touch-down amplification was performed with an initial step of 95°C for 15 min, followed by 7 cycles of 95°C for 30s, annealing temperatures starting at 66°C for 45s (decreasing by 0.5°C/cycle), and 74°C for 45s for extension. This step was followed by 30 cycles of 95°C for 30s, 63°C for 45s and 74°C for 45s. A novel allele was subsequently validated by cloning and sequence analysis as described in detail in **Chapter 2**.

7.2.4 Nomenclature

Throughout this chapter, gene accession number was adopted.

7.2.5 Phylogenetic Analysis

A compilation of a representative number of sheep, cattle and goat DQB2 sequences was carried out (**Appendix 3**). However, no goat DQB2 sequences were available in the database. The GenBank accession numbers of the sequences for phylogenetic analysis were: the sheep DQB2 found in this study (**Table 37**) and the cattle DQB2 sequences: U77796-98 (Sigurdardottir et al. 1992). A phylogenetic tree was rooted with the human DQB2 sequence HLA-DQB2 *0101 (M24921; Tiercy et al. 1989) as an out group. A neighbour-joining tree (Saitou & Nei 1987) was constructed on the basis of genetic distances, estimated by the Kimura (1980) two-parameter method, using the MEGA program. GenBank sequences were trimmed to the lengths corresponding to the PCR amplimers before generating the neighbour-joining tree.

7.3 Results

7.3.1 Sequence Polymorphisms of the Second Exon of Ovar-DQB2

A total number of 235 Texel DNA samples were genotyped for Ovar-DQB2. Using JM05/JM07 amplimers, 277 bp were obtained from the sheep DNA. Under the established conditions, a total of 16 Ovar-DQB2 alleles including a null allele were identified from Texel lambs (**Table 37**).

Table 37 Nomenclature of Ovar-DQB2 alleles detected in Texel lambs in this study

Local name	Accession Number
DQB*16	AJ238934
DQB*17	AJ238935
DQB*25	AJ238943
DQB*28	AJ238946
4389	GU191459
NewAllele2	HM367630
NewAllele3	HM367631
HQ728669	HQ728669
8t013	LN868258
8t023	LN868259
0t041	LN868260
0t175	LN868261
Null	NA
OAU07032	U07032
OAU07033	U07033
Z28424	Z28424

In this chapter, the nucleotide and amino acid variations obtained from the first set of primers were analysed. There were nucleotide and amino acid variations among 16 DQB2 alleles found in this study. Sixty-two of the 233 nucleotide sites (26.6%) analysed in this study were polymorphic (**Figure 27**). An alignment of the deduced amino acid sequence encoded by exon 2 is shown in **Figure 28**. 44.9% amino acid polymorphic sites were identified (35 out of 78) (**Table 38**). The highest number of substitutions was found in amino acid residues β 14 (H, L, Q), β 28 (K, N, T), β 30 (N, Q, Y), β 45 (D, G, N), β 47 (F, H, Y) and β 56 (P, Q, R) with three different amino acid per sites, and in residues β 9 (F, H, V, Y), β 26 (L, H, S, Y) and α 37 (D, F, H, Y) with four. Interesting to note also, there were five amino acids observed in residue β 57 (D, E, H, Q, S) and β 85 (A, G, L, N, V). Not all amino acid sites that were included in the putative peptide-binding region were variable in this population. For example, residues β 15, β 26, β 48, β 78, β 79 and β 83 were not variable.

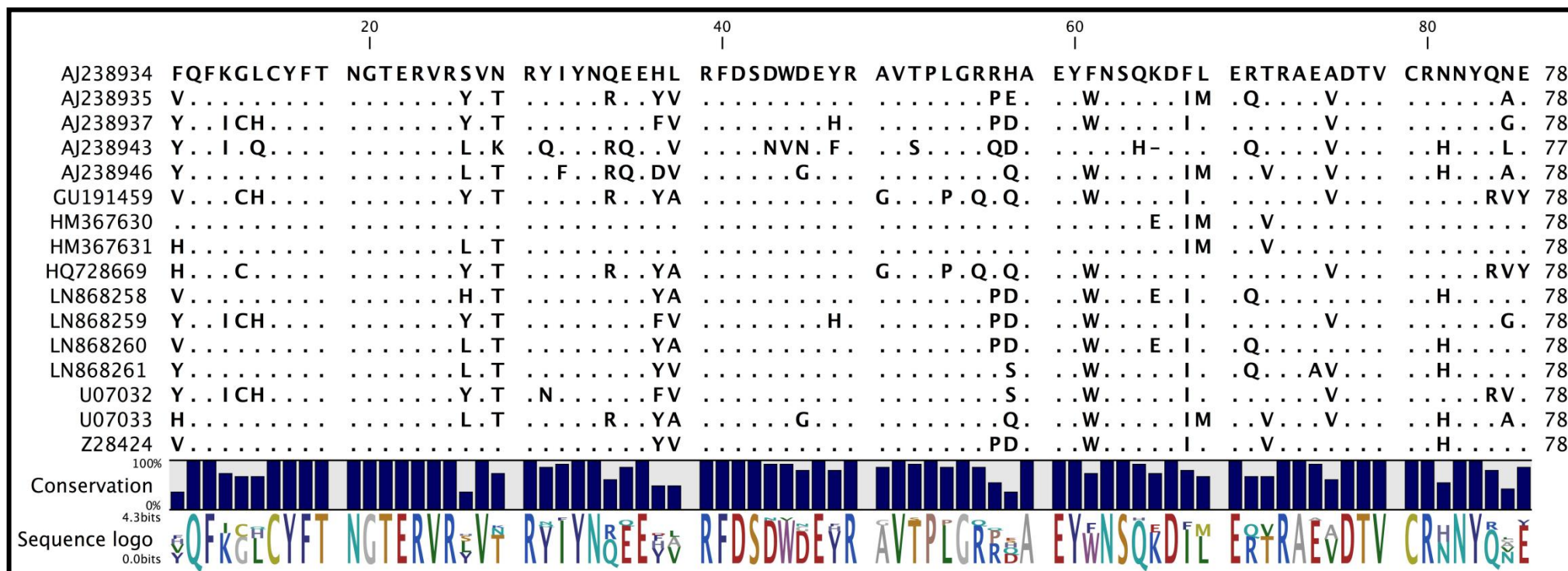


Figure 28 The distribution of polymorphisms within amino acid translations of the second exon of DQB2 found in this study. A dot indicates identity with the top sequence, AJ238934.

Table 38 Amino acid variations in Texel sheep in this study. Amino acid positions involved in the antigen binding sites according to Reche & Reinherz (2003) are indicated by grey background.

Amino Acid Position	Texel in this study
9	F, H, V, Y
12	I, K
13	C, G
14	H, L, Q
26	H, L, S, Y
28	K, N, T
30	N, Q, Y
31	F, I
34	Q, R
35	E, Q
37	D, F, H, Y
38	A, L, V
43	D, N
44	N, W
45	D, G, N
47	F, H, Y
49	A, G
51	S, T
53	L, P
55	Q, R
56	P, Q, R
57	D, E, H, Q, S
61	F, W
64	H, Q
65	E, K
67	F, I
68	L, M
70	Q, R
71	T, V
74	A, E
75	A, V
81	H, N
84	Q, R
85	A, G, L, N, V
86	E, Y

7.3.2 Frequencies of the Ovar-DQB2 Alleles

The frequencies of each allele in Texel are shown in **Table 39**. The most frequent DQB2 allele in Texel is null (21.1%), followed by AJ238935 (18.3%) and LN868259 (15.7%). Four rare alleles; AJ238934, HM367630, U07032 and Z28424 were detected; each had a frequency of less than 1% in this Texel population.

Table 39 Ovar-DQB2 and their frequencies found in Texel in the present study

Allele	Number	Frequency (%)	SE	95 CI (%)	
				Lower	Upper
AJ238934	2	0.43	0.30	0.00	1.06
AJ238935	86	18.30	1.74	15.11	21.49
AJ238943	8	1.70	0.59	0.64	2.77
AJ238946	25	5.32	1.05	3.40	7.23
HM367630	2	0.43	0.30	0.00	1.06
HM367631	37	7.87	1.19	5.53	10.43
HQ728669	5	1.06	0.47	0.21	2.13
LN868258	26	5.53	1.07	3.62	7.45
LN868259	74	15.74	1.68	12.55	18.94
LN868260	59	12.55	1.62	9.36	15.74
LN868261	31	6.60	1.18	4.26	9.15
LN868264	5	1.06	0.47	0.21	2.13
Null	99	21.06	1.82	17.66	24.68
U07032	4	0.85	0.42	0.21	1.70
U07033	6	1.28	0.51	0.43	2.34
Z28424	1	0.21	0.21	0.00	0.64

7.3.3 Comparison of Diversity and Frequencies between DQB1 and DQB2

Figure 29 exhibits the comparison of allele diversity and frequencies between DQB1 and DQB2 in this study. There were a total of 16 DQB2 alleles compared to 13 DQB1 alleles for DQB1.

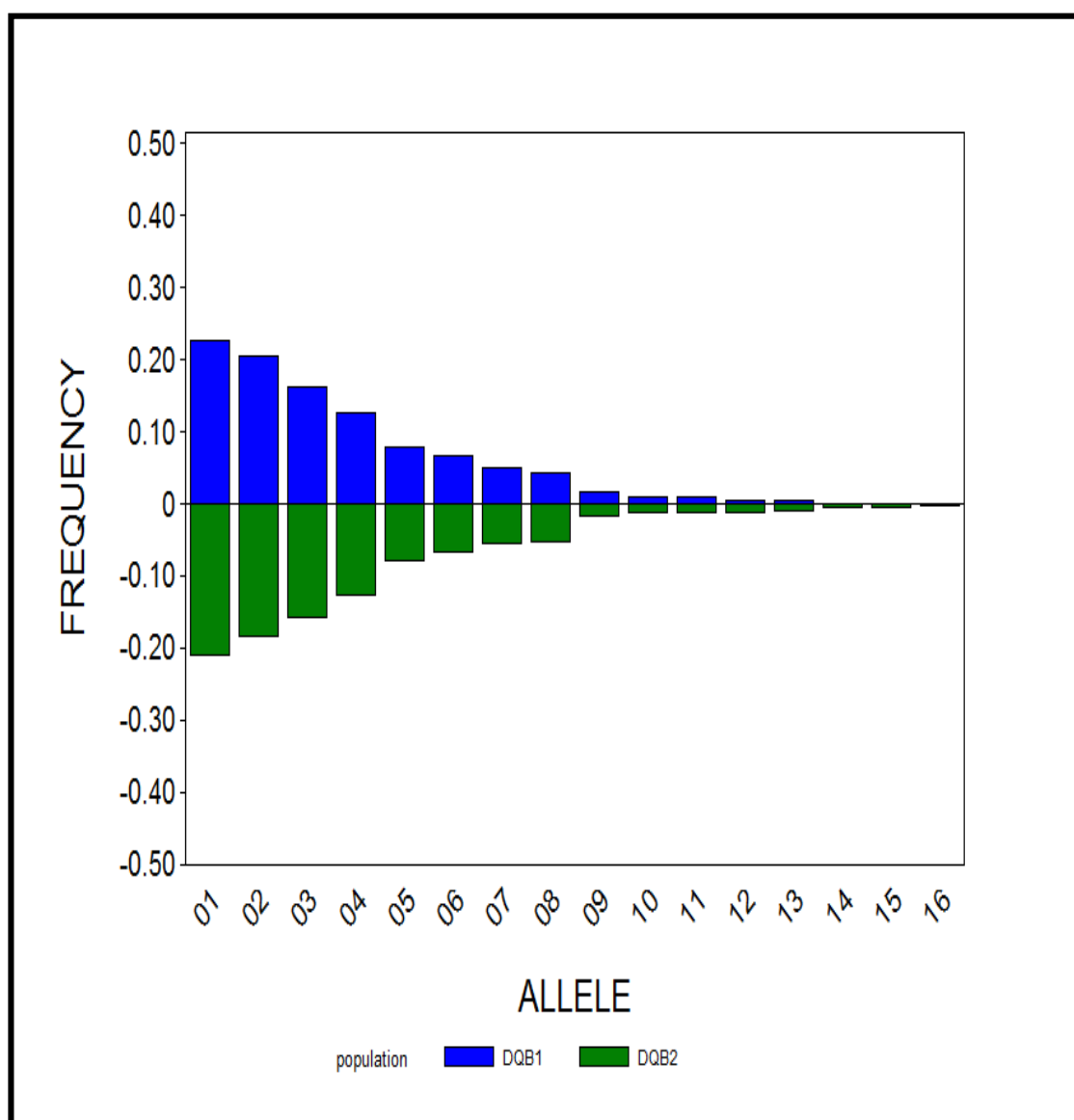


Figure 29 A comparison between diversity and frequencies between DQB1 and DQB2 in Texel

7.3.4 Phylogenetic analysis among of the Ovar-DQB Alleles

A phylogenetic tree was constructed from exon 2 of the Ovar-DQB2 and Ovar-DQB1 (from **chapter 5**) from this study revealing six main branches. Some sheep DQB1 alleles sequences were found clustered with more DQB2 sequences than DQB1 (**Figure 30**).

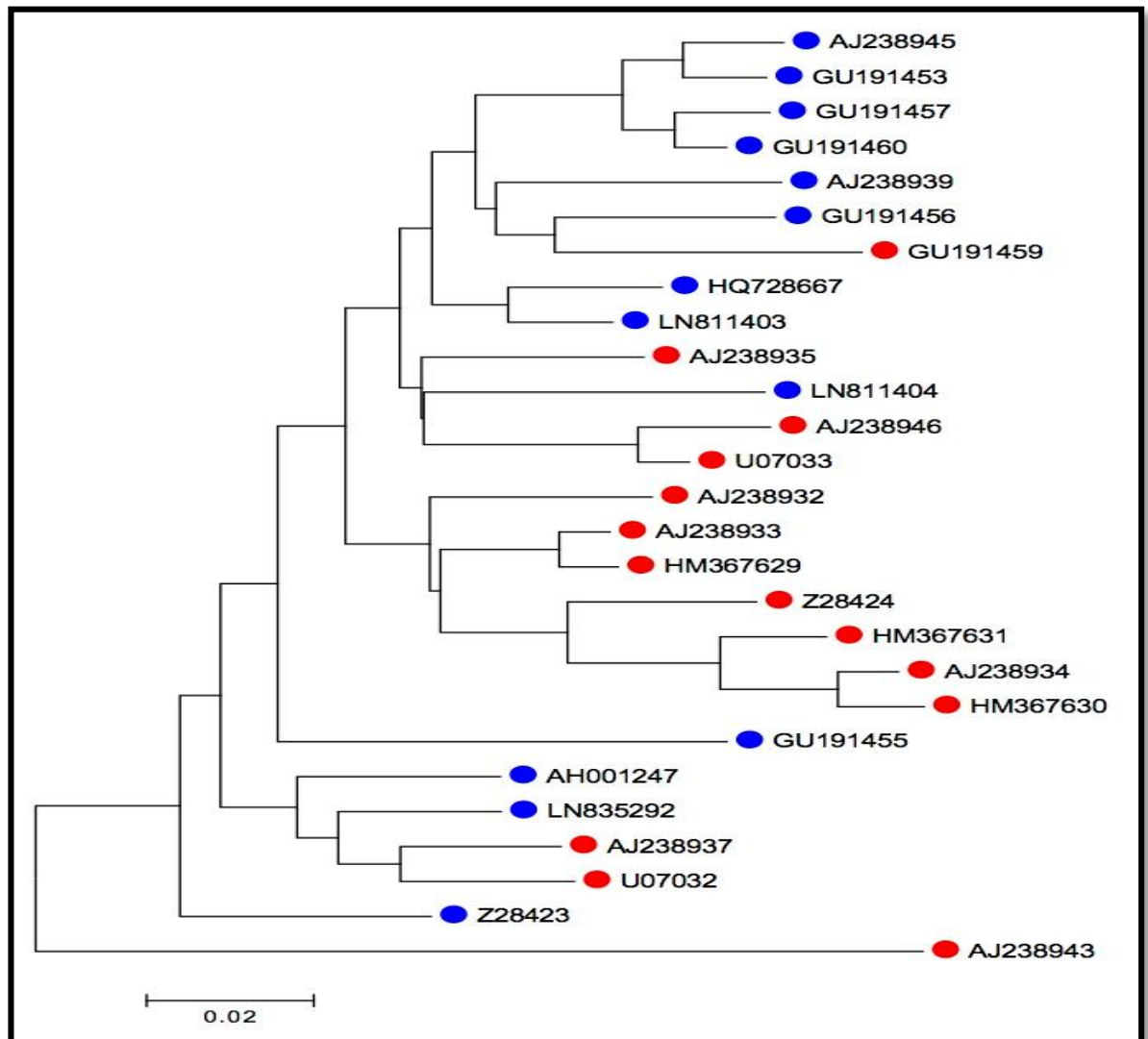


Figure 30 A neighbor-joining phylogenetic tree constructed from exon 2 sequences of DQB1 and DQB2 genes from Texel sheep in this study. Branch lengths are proportional to genetic distance. The blue and red symbols denote Ovar-DQB1 and Ovar-DQB2 respectively.

7.4 Discussion

In this chapter, the polymorphisms of Texel DQB2 were successfully characterized by sequence-based typing. The Ovar-DQB2 DNA nucleotide sequence was 233 bp long and encoded 78 amino acids. 16 DQB2 alleles were amplified from Texel population. The sheep DQB2 nucleotides and amino acid sequences also displayed variability at many positions. The most frequent DQB2 allele was null followed by AJ238935. The phylogenetic analysis has shown that some sheep DQB2 alleles share similar lineage with DQB1 alleles.

Our particular interest is amplification of the second exon of DQB2. The first set of primers, JM05/JM07 amplifies most of DQB2 alleles except AJ2389435 and AJ238946 alleles in some heterozygote samples. Preferential amplification of one allele instead of two alleles in heterozygote animal occurs in PCR reaction (Snibson et al. 1998). Subsequently, the other set of primer (1005/1007) was designed to overcome this problem. In addition, the new primer pair which binds in the intron regions enables the amplification for the whole exon 2. However, this primer set amplified the non-MHC allele. A third primer, which was modified from JM05/07 primer sequence, was designed. The two alleles were successfully amplified through usage of the third primer set.

The diversity of DQB2 gene in Texel sheep was also analysed. 16 different sequences including null were obtained from sequence analysis. Five of these were newly identified sequences. The variability of Ovar-DQB2 found in this Texel population suggests that the Ovar-DQB2 is one of a polymorphic locus in MHC class II (Dukkipati et al. 2006b). The level of diversity detected for the Texel DQB2 locus appears to be higher than DQB1, DQA1, and DQA2. However, DQB2 diversity was lower compared with DRB1 in this population.

Almost half (44.9%) amino acid sites were polymorphic sites in sheep DQB2 molecules. These polymorphic sites share patterns of clustering and similar amino acid substitutions were described in DQB1 of previous chapter, suggesting that polymorphism at the DQB1 and DQB2 loci has been conserved in sheep. We have identified 15 polymorphic positions at the peptide binding region of the sheep DQB2

molecule. Two of these polymorphic positions (position 57 and 85) appeared with five amino acids substitution. This five amino acid substitution were not observed with DQB1.

7.5 Conclusion

This study provides information on the diversity of Texel DQB2, information that can assist in the search of associations with disease resistance. Sequence-based typing can be used in future to determine the diversity of DQB2 in other breeds.

CHAPTER 8

MHC CLASS IIa HAPLOTYPES AND LINKAGE DISEQUILIBRIUM IN TEXEL

8.0 Summary

In this chapter, the genomic sequences information of 235 Texel obtained from sequence-based typing were used to investigate the haplotype and linkage disequilibrium pattern of Texel MHC class IIa genes. It was shown that the Texel MHC class IIa is characterized by only 21 distinct DR-DQ haplotypes which illustrates extreme non-random haplotypic association of alleles at these loci. The number of DQ genes per haplotype varies among this population. In addition, total linkage disequilibrium values were observed between some MHC class IIa alleles.

8.1 Introduction

MHC class II molecules are known to play a significant role in regulation of host immune response in susceptibility to specific diseases and tissue transplantation. These molecules are cell membrane-integrated glycoproteins, which are expressed on the surface antigen presenting cells such as dendritic cells, B cells and macrophages. In sheep, the class II molecules are encoded by DR and DQ genes located at the MHC class IIa region chromosome 20. Thus, the basic genetic and genomic structures of MHC class IIa have been of great interest to many researchers.

The MHC class IIa genomic structure has been studied in two breeds and they differ. A study using the bacterial artificial chromosome (BAC) DNA library of a Rambouillet ram has confirmed that MHC class IIa consist one DRB1 gene, two DQA genes (DQA1 and DQA2) and two DQB (DQB1 and DQB2) genes (Herrmann-Hoesing et al. 2008b). A similar pattern was observed in Merino sheep except with the absence of DQB2 gene (Liu et al. 2006).

The presence of two DQA genes is in agreement with the work of Hickford and co-workers (2007). They showed that at the DNA level, present in both combination of DQA1 and DQA2 genes or DQA2 and DQA2-like genes per haplotype. Recently, Ballingall et al. (2015) has provided for support this fact, by demonstrating of two DQA genes per haplotype in the transcript of Prealpe sheep. So far, no report relating to haplotype is available for Texel breed. The haplotype of MHC class IIa in the Texel population was identified through coinheritance from family data in this chapter.

Linkage disequilibrium defines the non-random association of alleles between two loci. The genetic studies of animals has been focussed on the extent of linkage disequilibrium because the knowledge is vital in localizing QTL affecting outcome of infectious diseases or economically important traits. This linkage disequilibrium could be due to result of multiple genetic and molecular factors (Ardlie et al. 2002) and the high linkage disequilibrium frequently observed on domestic animals as compared to humans is due to forces such as admixture, genetic drift and small effective size (McRae et al. 2002). In the human and cattle MHC, strong linkage disequilibrium is established between DR-DQ regions (Anderson & Rask, 1986). It is interesting to see if strong

linkage disequilibrium is also observed in sheep MHC (Stear et al. 1996). The primary aim of this chapter therefore is to establish the linkage disequilibrium pattern between DR-DQ loci specifically in Texel population. This study also can further enhance the knowledge concerning the actual gene that is responsible for certain diseases.

8.2 Materials and Methods

8.2.1 Haplotype Determination

The sequence-based typing method (as described in Chapters 3-7) does not determine specific haplotypes but instead shows what alleles of DRB1, DQA1, DQA2, DQA2-like, DQB1 and DQB2 sequences a sheep carries. The haplotypes were determined from coinheritance sequences of sire, dam and their siblings (see section 2.5.2). For convenience, the haplotypes are identified with a prefix “#” followed by a letter. The haplotype frequencies were determined by the PROC ALLELE procedure in SAS.

8.2.2 Linkage Disequilibrium

A variety of linkage disequilibrium measures are available in literature and the best parameter depends on the objectives (McRae et al. 2002). Linkage disequilibrium was reported using two parameters in this chapter. The correlation coefficient (r) and the standardised linkage disequilibrium coefficient (D') were determined between all pairs of alleles for each pair of loci. These two LD measures, r^2 and D' are common parameter for linkage disequilibrium in association studies (Thomson & Single 2014). However, the r^2 is preferred to D' for measuring and comparing linkage disequilibrium in the context of gene mapping (Thomson & Single 2014). Linkage disequilibrium was measured by the **ALLELE** procedure in SAS.

8.3 Results

8.3.1 Texel MHC class II Haplotypes and Their Frequencies

Although 235 independent sheep were examined, only 21 DR-DQ haplotypes were identified in this Texel flock (**Table 40**). Consequently, most of the DRB1 alleles in this sample have exclusive association with one specific DQA-DQB combination. There are three DRB1 alleles (FR686849, G2 and M), however, which are associated with more than one specific DQA-DQB combination. The FR686849 is found with two different DQA1, DQB1 and DQA2 alleles but with only one DQA2-like and DQB2, while the G2 allele is found with DQA1*Null-DQB1*Null-DQA2*AY312375-DQA2-like*AY312392 but having two different DQB2 alleles, AJ238935 and AJ238946. The M allele, which is the most common DRB1 allele found in this population, is found with DQA1*M33304-DQB1*GU191455 and GU191459-DQA2*AY312382-DQA2-like* Null -DQB2*Null in 99 of 101 animals. In two animals however, it is found with DQA1*LN827890-DQB1*GU191457-DQA2*AY31287-DQA2-like*Null-DQB2*AJ238934 whereas, U00219 and FM998807 share similar DQA-DQB alleles.

The DR-DQ haplotype frequencies vary from 0.4-21.1% in this Texel flock (**Table 40**). The most frequent Texel DR-DQ haplotypes were #p (21.1%), followed with #ka (15.1%) and #m (13.2%). In contrast, six rare haplotypes (#e, #f, #h, #j, #s and #t) were recorded in less than 1%. All other twelve haplotypes had a frequencies ranging from 1 to 13%.

The total number of loci per haplotypes varied among sheep. The majority of haplotypes observed in this flock consisted of two DQA and two DQB genes per haplotype. However, four haplotypes namely #g, #h, #ka and #kb were different. The haplotype #g has three sets of DQA and DQB genes, while the haplotype #h consists of two DQA and three DQB genes. Interestingly, the haplotype #ka and #kb consist of only two DQA and one DQB gene per haplotype.

Table 40 MHC class IIa haplotypes of Texel sheep in this study

Haplotype	DRB1	DQA1	DQA2	DQA2-like	DQB1	DQB2	n	Frequency	SE	(%)	
										Lower	Upper
#a	A	LN827891	AY312388	Null	AJ238939	LN868261	31	6.60	1.18	4.26	9.15
#b	B2	M33304	AY312377	Null	AH001247	AJ238935	15	3.19	0.85	1.70	4.89
#c	C2	LN827894	AY312381	Null	Z28423	HQ728669	5	1.06	0.47	0.21	2.13
#d	D2	LN827892	AY312381	Null	GU191456	LN868260	59	12.55	1.62	9.36	15.74
#e	DQ659115	LN827893	AY312386	Null	LN811403	OAU07032	4	0.85	0.42	0.21	1.70
#f	FN393738	LN827890	AY312387	Null	GU191453	HM367630	2	0.43	0.30	0.00	1.06
#g	FN534114	M33304	AY312375	AY312392	GU191455(GU191459)	OAU07033	6	1.28	0.51	0.43	2.34
#h	FN870432	LN827891	AY312382	Null	GU191455(GU191459)	Z28424	1	0.21	0.21	0.00	0.64
#i	FR686849	LN736359	AY312389	Null	AJ238945	LN868258	6	1.28	0.51	0.43	2.34
#j	FR686849	M33304	AY312377	Null	HQ728667	LN868258	2	0.43	0.30	0.00	1.06
#ka	G2	Null	AY312375	AY312392	Null	AJ238935	71	15.11	1.61	12.13	18.30
#kb	G2	Null	AY312375	AY312392	Null	AJ238946	25	5.32	1.05	3.40	7.23

Haplotype	DRB1	DQA1	DQA2	DQA2- like	DQB1	DQB2	n	Frequency	SE	(%)	
										Lower	Upper
#l	GSF	LN827890	AY312387	Null	GU191460	HM367631	37	7.87	1.19	5.53	10.43
#m	H3	M33304	AY312377	Null	HQ728667	LN868259	62	13.19	1.59	10.00	16.17
#n	HG515541	M33304	AY312377	Null	AH001247	LN868264	5	1.06	0.47	0.21	2.13
#o	L	LN736359	AY312389	Null	AJ238945	LN868258	18	3.83	0.92	2.13	5.53
#p	M	M33304	AY312382	Null	GU191455 (GU191459)	Null	99	21.06	1.82	17.66	24.68
#q	TUV	Null	AY312375	AY312392	LN811404	AJ238943	8	1.70	0.59	0.64	2.77
#r	U00219	M33304	AY312377	Null	HQ728667	LN868259	10	2.13	0.66	0.85	3.40
#s	FM998807	M33304	AY312377	Null	HQ728667	LN868259	2	0.43	0.30	0.00	1.06
#t	M	LN827890	AY312387	Null	GU191457	AJ238934	2	0.43	0.30	0.00	1.06

8.3.2 Linkage Disequilibrium among MHC Class II Loci

Table 41 lists linkage disequilibrium parameters between the DRB1 and other MHC class IIa loci, DQA1, DQB1, DQA2, DQA2-like and DQB2. It can be seen clearly that there is strong linkage disequilibrium between several alleles. The r and D' values are different for each DR-DQ haplotype. The complete positive linkage disequilibrium value ($r=1$) was observed in haplotypes; DRB1*0401-DQA1*LN827894, DRB1*1601-DQA1*LN827892, DRB1*0401-DQB1*Z28423, DRB1*0701-DQB1*LN811404, DRB1*0901-DQB1*AJ238939, DRB1*1101-DQB1*Null, DRB1*1401-DQB1*GU191460, DRB1*1601-DQB1*GU191456, DRB1*0901-DQB1*1001, DRB1*0401-DQB2*GU191459, DRB1*0701-DQB2*AJ238943, DRB1*0901-DQB2*LN868261, DRB1*1601-DQB2*LN868260, DRB1*FN543114-DQB2*U07033 and DRB1*HQ515541-DQB2*LN868264. On the other hand, the haplotype DRB1*0201-DQB2*Null had the highest D' value (0.1654).

Table 41 Linkage disequilibrium between DRB1 and other MHC class IIa genes

Locus1	Locus 2	n	Frequency	r	D'
DRB1-DQA1					
0102	M33304	62	13.19	0.4510	0.0755
0201	M33304	99	21.06	0.5843	0.1187
0302	LN736359	18	3.83	0.8603	0.0383
0401	LN827894	5	1.06	1.0000	0.0105
0601	M33304	15	3.19	0.0210	0.0183
0701	Null	8	1.70	0.2469	0.0133
0901	LN827891	31	6.60	0.9831	0.0615
1101	Null	96	20.43	0.9504	0.1591
1401	LN827890	37	7.87	0.9456	0.0719
1601	LN827892	59	12.55	1.0000	0.1098
FN543114	M33304	6	1.28	0.1316	0.0073
FR686849	LN736359	6	1.28	0.4178	0.0119
HQ515541	M33304	5	1.06	0.1200	0.0061
U00219	M33304	10	2.13	0.1706	0.0122
DRB1-DQB1					
0102	HQ728667	62	13.19	0.8876	0.1106
0201	GU191455	99	21.06	0.9447	0.1622
0302	AJ238945	18	3.83	0.8603	0.0363
0401	Z28423	5	1.06	1.0000	0.0105
0601	AH001247	15	3.19	0.8613	0.0306
0701	LN811404	8	1.70	1.0000	0.0167
0901	AJ238939	31	6.60	1.0000	0.0616
1101	Null	96	20.43	1.0000	0.1625
1401	GU191460	37	7.87	1.0000	0.0725
1601	GU191456	59	12.55	1.0000	0.1098
FN543114	GU191455	6	1.28	0.2107	0.0099
FR686849	AJ238945	6	1.28	0.4178	0.0119
HQ515541	AH001247	5	1.06	0.4919	0.0102
U00219	HQ728667	10	2.13	0.3357	0.0178
DRB1-DQA2					
0102	0103	62	13.19	0.7694	0.1050
0201	0602	99	21.06	0.9810	0.1649
0302	1101	18	3.83	0.8603	0.0363
0401	0601	5	1.06	0.2612	0.0092
0601	0103	15	3.19	0.3584	0.0254
0701	0101	8	1.70	0.2381	0.0130
0901	1001	31	6.60	1.0000	0.0616
1101	0101	96	20.43	0.9165	0.1565
1401	0901	37	7.87	0.9456	0.0719
1601	0601	59	12.55	0.9543	0.1084
FN543114	0101	6	1.28	0.2057	0.0098
FR686849	1101	6	1.28	0.4178	0.0119
HQ515541	0103	5	1.06	0.2047	0.0085
U00219	0103	10	2.13	0.2910	0.0169
DRB1-DQA2-like					
0102	Null	62	13.19	0.2155	0.0309
0201	Null	101	21.49	0.2892	0.0503

Locus1	Locus 2	n	Frequency	r	D'
0302	Null	18	3.83	0.1103	0.0090
0401	Null	5	1.06	0.0573	0.0025
0601	Null	15	3.19	0.1004	0.0075
0701	1401	8	1.70	0.2381	0.0130
0901	Null	31	6.60	0.1469	0.0154
1101	1401	96	20.43	0.9165	0.1565
1401	Null	37	7.87	0.1616	0.0184
1601	Null	59	12.55	0.2094	0.0294
FN543114	1401	6	1.28	0.2057	0.0098
FR686849	Null	8	1.70	0.0727	0.0040
HQ515541	Null	5	1.06	0.0573	0.0025
U00219	Null	10	21.3	0.0815	0.0050
DRB1-DQB2					
0102	LN868259	62	13.19	0.9013	0.1111
0201	Null	99	21.06	0.9874	0.1654
0302	LN868258	18	3.83	0.8247	0.0362
0401	GU191459	5	1.06	1.0000	0.0105
0601	AJ238935	15	3.19	0.3837	0.0261
0701	AJ238943	8	1.70	1.0000	0.0167
0901	LN868261	31	6.60	1.0000	0.0616
1101	AJ238935	71	15.11	0.7293	0.1137
1101	AJ238946	25	5.32	0.4678	0.0423
1401	HM367631	37	7.87	1.0000	0.0725
1601	LN828260	59	12.55	1.0000	0.1098
FN543114	U07033	6	1.28	1.0000	0.0126
FR686849	LN868258	8	1.70	0.5488	0.0161
HQ515541	LN868264	5	1.06	1.0000	0.0105
U00219	LN868259	10	2.13	0.3411	0.0179

Table 42 shows linkage disequilibrium between the DQA1 and other genes (DQB1, DQA2, DQA2-like and DQB2). Similar observation in **Table 41** shows there was strong linkage disequilibrium between several alleles, which r and D' values are different. The $r=1$ was observed in seven haplotypes including DQA1*LN736359-DQB1*AJ238945, DQA1*LN827892-DQB1*GU191456, DQA1*LN827894-DQB1*Z28423, DQA1*LN736359-DQA2*1101, DQA1*LN827890-DQA2*0901, DQA1*LN827892-DQB1*LN868260 and DQA1*LN827894-DQB1*GU191459. On the other hand, two haplotypes; DQA1*Null-DQA2*0101 and DQA1*Null-DQA2*1401 had the highest positive D' (0.1695).

Table 42 Linkage disequilibrium between DQA1 and other MHC class IIa genes (DQB1, DQA2, DQA2-like and DQB2 genes)

Locus 1	Locus 2	n	Frequency	r	D'
DQA1-DQB1					
LN736359	AJ238945	24	5.11	1.0000	0.0485
LN827890	GU19140	37	7.87	0.9456	0.0719
LN827891	AJ238939	31	6.60	0.9831	0.0615
LN827892	GU191456	59	12.55	1.0000	0.1098
LN827894	Z28423	5	1.06	1.0000	0.0105
M33304	AH001247	20	4.26	0.2439	0.0244
M33304	GU191455	105	22.34	0.6140	0.1270
M33304	HQ728667	76	16.17	0.5081	0.0925
Null	LN811404	8	1.70	0.2469	0.0133
Null	Null	96	20.43	0.9504	0.1591
DQA1-DQA2					
LN736359	1101	24	5.11	1.0000	0.0485
LN827890	0901	41	8.72	1.0000	0.0796
LN827891	1001	31	6.60	0.9831	0.0615
LN827892	0601	59	12.55	0.9543	0.1084
LN827894	0601	5	1.06	0.2612	0.0092
M33304	0101	6	1.28	-0.4169	-0.0873
M33304	0103	96	20.43	0.5861	0.1169
M33304	0602	99	21.06	0.5909	0.1196
Null	0101	104	22.13	0.9643	0.1695
DQA1-DQA2-like					
LN736359	Null	24	5.11	0.1282	0.0120
LN827890	Null	41	8.72	0.1709	0.0204
LN827891	Null	32	6.81	0.1494	0.0159
LN827892	Null	59	12.55	0.2094	0.0294
LN827894	Null	5	1.06	0.0573	0.0025
M33304	1401	6	1.28	-0.4169	-0.0873
M33304	Null	195	41.49	0.4169	0.0873
Null	1401	104	22.13	0.9643	0.1695
DQA1-DQB2					
LN736359	LN868258	24	5.11	0.9586	0.0482
LN827890	HM367631	37	7.87	0.9456	0.0719
LN827891	LN868261	31	6.60	0.9831	0.0615
LN827892	LN868260	59	12.55	1.0000	0.1098
LN827894	GU191459	5	1.06	1.0000	0.0105
M33304	AJ238935	15	3.19	-0.2422	-0.0463
M33304	LN868259	74	15.74	0.5001	0.0901
Null	LN868264	5	1.06	0.1200	0.0061
M33304	Null	99	21.06	0.5976	0.1206
M33304	U07033	6	1.28	0.1316	0.0073
Null	AJ238935	71	15.11	0.6889	0.1106
Null	AJ238943	8	1.70	0.2469	0.0133
Null	AJ238946	25	5.32	0.4446	0.0414

Similar analysis between the DQB1 and DQA2, DQA2-like and DQB2 shows that the r and D' values are varies (**Table 43**). The haplotypes DQB1*AJ238939-DQA2*1001, DQB1*AJ238945-DQA2*1101, DQB1*AJ238939-DQA2*LN868261, DQB1*GU191456-DQB2*LN828260, DQB1*GU191460-DQB2*HM367631, DQB1*LN811404-DQB2*AJ238943, DQB1*Z28423-DQB2*GU191459 have $r=1$. On the other hand, the haplotype DQB1*GU191455-DQA2*0602 pose highest positive D' (0.1648).

Table 43 Linkage disequilibrium between DQB1 and DQA2, DQA2-like and DQB2

Locus 1	Locus 2	n	Frequency	r	D'
DQB1-DQA2					
AH001247	0103	20	4.26	0.4161	0.0339
AJ238939	1001	31	6.60	1.0000	0.0616
AJ238945	1101	24	5.11	1.0000	0.0485
GU191455	0101	6	1.28	-0.2262	-0.0400
GU191455	0602	100	21.28	0.9634	0.1648
GU191456	0601	59	12.55	0.9543	0.1084
GU191460	0901	37	7.87	0.9456	0.0719
HQ728667	0103	76	16.17	0.8669	0.1287
LN811404	0101	8	1.70	0.2381	0.0130
Null	0101	96	20.43	0.9165	0.1565
Z28423	0601	5	1.06	0.2612	0.0092
DQB1-DQA2-like					
AH001247	Null	20	4.26	0.1165	0.0100
AJ238939	Null	31	6.60	0.1469	0.0154
AJ238945	Null	24	5.11	0.1282	0.0120
GU191455	1401	6	1.28	-0.2262	-0.0400
GU191455	Null	100	21.28	0.2262	0.0400
GU191456	Null	59	12.55	0.2094	0.0294
GU191460	Null	37	7.87	0.1616	0.0184
HQ728667	Null	76	16.17	0.2428	0.0378
LN811404	1401	8	1.70	0.2381	0.0130
Null	1401	96	20.43	0.9165	0.1565
Z28423	Null	5	1.06	0.0573	0.1025
DQB1-DQB2					
AH001247	AJ238935	15	3.19	0.3092	0.0241
AH001247	LN868264	5	1.06	0.4919	0.0102
AJ238939	LN868261	31	6.60	1.0000	0.0616
AJ238945	LN868258	24	5.11	0.9586	0.0482
GU191455	Null	99	21.06	0.9573	0.1631
GU191455	U07033	6	1.28	0.2107	0.0099
GU191456	LN828260	59	12.55	1.0000	0.1098
GU191460	HM367631	37	7.87	1.0000	0.0725
HQ728667	LN868259	74	15.74	0.9843	0.1320
LN811404	AJ238943	8	1.70	1.0000	0.0167
Null	AJ238935	71	15.11	0.7293	0.1137
Null	AJ238946	25	5.32	0.4678	0.0423
Z28423	GU191459	5	1.06	1.0000	0.0105

Table 44 shows similar analysis, with the table referring to linkage disequilibrium values between the DQA2 with DQA2-like and DQB2, together with the linkage disequilibrium value between DQA2-like and DQB2. Only two consecutive haplotypes had complete perfect positive linkage disequilibrium; DQA2*0101-DQA2-like*1401 and DQA2*1001-DQB2*LN868261. The highest positive D' observed in DQA2*0101-DQA2-like*1401 and DQA2-like*0101-DQB2*AJ238935 (the D' values are 0.1793 and 0.1082 respectively).

Table 44 Linkage disequilibrium between DQA2 and DQA2-like and DQB2; DQA2-like and DQB2

Locus 1	Locus 2	n	Frequency	r	D'
DQA2-DQA2-like					
0101	1401	110	0.2340	1.0000	0.1793
0103	Null	96	0.2043	0.2810	0.0478
0601	Null	64	0.1362	0.2195	0.0319
0602	Null	100	0.2128	0.2874	0.0498
0901	Null	41	0.0872	0.1709	0.0204
1001	Null	31	0.0660	0.1469	0.0154
1101	Null	24	0.0511	0.1282	0.0120
DQA2-DQB2					
0101	AJ238945	71	0.1511	0.6612	0.1082
0101	AJ238943	8	0.0170	0.2381	0.0130
0101	AJ238946	25	0.0532	0.4288	0.0407
0101	U07033	6	0.0128	0.2057	0.0098
0103	AJ238935	15	0.0319	-0.0350	-0.0055
0103	LN868259	74	0.1594	0.8532	0.1253
0103	LN868264	5	0.0106	0.2047	0.0085
0601	GU191459	5	0.0106	0.2612	0.0092
0601	LN828260	59	0.1255	0.9543	0.1084
0602	Null	99	0.2106	0.9936	0.1658
0901	HM367631	37	0.0787	0.9456	0.0719
1001	LN868261	31	0.0660	1.0000	0.0616
1101	LN868258	24	0.0511	0.9586	0.0482
DQA2-like-DQB2					
1401	AJ238935	71	0.1511	0.6612	0.1082
1401	AJ238943	8	0.0170	0.2381	0.0130
1401	AJ238946	25	0.0532	0.4288	0.0407
1401	U07033	6	0.0128	0.2057	0.0098
Null	AJ238935	15	0.0319	-0.6612	-0.1082
Null	GU191459	5	0.0106	0.0573	0.0025
Null	HM367631	37	0.0787	0.1616	0.0184
Null	LN868260	59	0.1255	0.2094	0.0294
Null	LN868258	26	0.0533	0.1338	0.0129
Null	LN868259	74	0.1574	0.2390	0.0368
Null	LN868261	31	0.0660	0.1469	0.0154
Null	LN868264	5	0.0106	0.0573	0.0025
Null	Null	99	0.2106	0.2855	0.0493

8.4 Discussion

The main objective of this chapter was to determine MHC class IIa haplotype and linkage disequilibrium pattern in a Texel flock. From 235 Texel sheep, only 21 haplotypes were identified and most of the DRB1 alleles had exclusive association with one specific DQA-DQB combination in this population. We found variation in the number of DQ genes per haplotypes. The most frequent haplotype in this study were DRB1*M-DQA1*M33304-DQB1*GU191455 and GU191459-DQA2*AY312382-DQA2-like*Null-DQB2*Null. Six rare haplotypes were observed with a frequency of less than 1% in this population.

It is interesting that given the observed polymorphism at the DR and DQ loci in this population (18, 8, 13, 8, 2 and 16 alleles for DRB1, DQA1, DQB1, DQA2 and DQA2-like and DQB2, respectively; see chapter 3-7), 479,232 different haplotypes are possible, and only 21 distinct haplotypes were observed from 235 Texel sheep. This very low number of haplotypes repertoire is expected due to the fact that the linkage disequilibrium is higher in domestic animals influenced by factors such as genetic drift, admixture, selection and small effective population sizes (McRae et al. 2002).

To our knowledge, this is the first study of the MHC class II in Texel which identifies and defines DR-DQ haplotypes by sequence-based typing together with pedigree information. MHC haplotype information for population studies offers advantages compared with single-locus, as a conservation of haplotypes (Hassan et al. 2011) and can enhance the statistical power of association test due to reduction in dimension (Clark 2004). The results presented here can also be used for the studying haplotype associated with diseases.

DQA and DQB genes per haplotype vary between sheep in this population. Majority of haplotypes obtained in this study consist of two DQA genes and two DQB genes per haplotype. This finding fits with the previous observation (Hickford et al. 2007; Ballingall et al. 2015) which suggest that the DQA consist of two genes per haplotype irrespective of combination of DQA1/DQA2 or DQA2/DQA2-like genes. However, in this investigation, three of the 21 haplotypes did not fit with this pattern, proposing that DQ gene number in sheep is variable. The variation in the number of DQA and DQB

gene per haplotype is reported in Spanish Churra sheep (Atlija et al. 2015) and in cattle (Ballingall et al. 1997; Sigurdardottir et al. 1998). This observation is unlikely due to PCR artefacts as six lambs pose similar pattern of haplotype. In addition, they come from different sire and dams.

Analysis of the distribution of haplotype frequencies revealed that the most common haplotype is #p, with more than 20 % of this Texel population having this haplotype. On the other hand, some of the rare haplotypes were observed at a frequency of less than 1%. The frequencies of MHC class II haplotype in this study can be used as a reference and also for purpose of comparing frequencies in other breeds or populations in MHC and disease studies.

No recombination events were observed between DR-DQ loci. This however is not surprising given the observation of high linkage disequilibrium among these two loci and the estimation of short physical distance between these genes (Dukkipati et al. 2006b). It is vital to note that some recombination could not be detected using the sequence-based typing as the alleles on both haplotypes were identical. Another interesting observation in this study was an ancient recombination observed among MHC class IIa genes in this population. The observation of ancient recombination is consistent with findings in DQA genes (Hickford et al. 2007; Ballingall et al. 2015). Ancient recombination is believed to be a mechanism that generates MHC diversity in sheep and other ruminants (Ballingall et al. 2015).

The report of linkage disequilibrium pattern between breeds offers an opportunity to disentangle the effects of alleles at closely linked loci in defining a causative mutation of nematode resistance (Stear et al. 2007). Two parameters of linkage disequilibrium have been reported in this study. The r and D' were determined between all pairs of alleles for each pair of loci. It seems that the two parameters yield different conclusions. Some previous reports suggest that DRB1 is also in linkage disequilibrium with MHC I region (Stear et al. 1996). It is possible that linkage disequilibrium extends to other MHC and non-MHC regions. The exact reason why linkage disequilibrium is high in sheep or farm animals has yet to be established.

Several pairs of alleles have complete linkage disequilibrium ($r=1$). The presence of strong linkage disequilibrium in MHC Class IIa has an important impact on MHC studies

and disease resistance including nematode resistance. For example, during an earlier investigation, one of DRB1 G2 allele has been associated with increased resistance to the nematode in Scottish Blackface. Another group working with Texel population failed to find association of the any DRB1 allele and nematode resistance. The haplotype analysis in this study indicates that DRB1*G2 occurs on two haplotypes (#ka and #kb), thus supporting the hypothesis that the other loci which in linkage disequilibrium with DRB1 locus can play an important role for disease resistance (Stear et al. 2005; Keane et al. 2007). However, this association of haplotype and nematode resistance will be discussed in the next chapter.

8.5 Conclusion

In conclusion, Texel MHC class IIa is characterized by low haplotype diversity and strong linkage disequilibrium between the loci. The number of DQ genes per haplotype varies between sheep in this Texel population.

CHAPTER 9

THE ASSOCIATION OF MHC CLASS IIa AND NEMATODE RESISTANCE IN TEXEL

9.0 Summary

An alternative control strategy for nematode problem in sheep is a breeding programme which selects genetically nematode resistance sheep. Identifying loci that are responsible for nematode resistance would simplify the selective breeding process. The objective of this chapter is to explore if any MHC class II haplotypes are associated with variation in nematode resistance. MHC class II haplotypes were determined by sequence-based typing assignment described in the previous chapters. All sheep were phenotypically assessed for nematode resistance by FEC and IgE activity against L3. The association of haplotypes and nematode resistance was estimated using mixed models. Two models were used, the first to determine the association of haplotypes and nematode resistance and the second to determine the association of haplotype homozygosity and nematode resistance. One haplotype, #d was associated with a decrease in FEC, while another haplotype, #l was associated with decrease in IgE activity against L3. There was no significant association between the effect of haplotype homozygosity and nematode resistance. The results suggest that the specific haplotype plays an important role in resistance to nematode infection in the Texel breed. This information adds new information to the existing knowledge regarding how the MHC controls nematode resistance in sheep.

9.1 Introduction

Gastrointestinal nematodes infection is a common problem in livestock. Traditionally, anthelmintic drugs are used to control the problem. However, due to occurrence of anthelmintic drug resistance in many farms, alternative measures are being explored and studied by scientists.

Different numbers of alternative measures have been proposed to replace the usage of anthelmintic drugs. These include protein supplementation, herbal drug usage, nematophagous fungi, development of nematode vaccines and selection of genetically nematode resistance sheep (Stear et al. 2007; Hoste & Torres-Acosta 2011). The evidence of success of genetic selection for nematode resistance in large livestock industries such as New Zealand and Australia, show the prospective value of this method for nematode control (Bisset et al. 2001; Stear et al. 2009). Selective breeding of sheep for nematode resistance not only lowers the requirement for anthelmintic control, it also reduces larval pasture contamination thus it diminishes the economic impact due to nematode infection.

Genetically resistant sheep have been identified phenotypically through egg excretion or FEC. However, FEC poses disadvantages which include low heritability, time-consuming, labour intensive processes and most importantly, the animal needs to encounter the parasitic challenge. Due to these disadvantages, genetic markers or DNA-based tests have been proposed, which could simplify the selective breeding process. In order to establish the use of genetic markers for nematode resistance, the fundamental step should be to identify loci responsible for nematode resistance (Stear et al. 2009).

MHC genes have been associated with resistance against nematodes (Stear et al. 2009). The association of MHC gene and nematode resistance is strongly established in previous reports (Schwaiger et al. 1995; Paterson et al. 1998; Buitkamp & Epplen 2001; Sayers et al. 2005; Stear et al. 2005; Davies et al. 2006; Keane et al. 2006; 2007; Castillo et al. 2011; Valilou et al. 2015). Schwaiger et al. (1995) have demonstrated that MHC class II genes influence nematode resistance of which the lambs with allele G2 has the lowest egg counts. A study on natural infection in Ireland has demonstrated that the

Texel breed is resistant compared to Suffolk based on FEC and nematode burden (Good et al. 2006) and further investigation of their MHC profile have shown the importance of allele G2 on nematode resistance in Suffolk breed, but not in the Texel (Sayers et al. 2005b). The result from this investigation suggests that other genes that are in linkage disequilibrium with allele G2 could also play significant roles in nematode resistance. This is in agreement with McCririe et al. (1997) and Stear et al. (1996). The involvement of other MHC genes in determining resistance phenotype is demonstrated in Keane et al. (2007) and Forrest et al. (2010) studies who discovered that DQA1 null was associated with susceptibility. To overcome this problem, haplotype association, instead of single gene could be the better approach (Forrest et al. 2010; Hassan et al. 2011). Therefore, the aim of this chapter is to determine the association between MHC class IIa haplotype and nematode resistance in a Texel flock.

9.2 Materials and Methods

9.2.1 Typing of MHC class IIa genes

Details of the methodology employed in typing have been described in **Chapter 3-7**.

9.2.2 Haplotypes Determination and Nomenclature

As described in **Chapter 8**, a total of 21 haplotypes were found in Texel population. From 21 haplotypes, only haplotypes that were present with gene frequency greater than 5% were included in the analysis of this chapter. For easy identification, each haplotype was given a distinct letter (**Table 45**).

Table 45 Haplotype nomenclature and their full haplotype description

No	Haplotypes
#a	DRB1*A- DQA1*LN827891- DQB1*AJ238939- DQA2*AY312388- DQA2-like*Null- DQB2*LN868261
#b	DRB1*B2- DQA1*M33304- DQB1*AH001247- DQA2*AY312377- DQA2-like*Null- DQB2*AJ238935
#d	DRB1*D2- DQA1*LN827892- DQB1*GU191456- DQA2*AY312381- DQA2-like*Null- DQB2*LN868260
#ka	DRB1*G2- DQA1*Null- DQB1*Null- DQA2*AY312375- DQA2-like*AY312392- DQB2*AJ238935
#kb	DRB1*G2-DQA1*Null-DQB1*Null-DQA2*AY312375-DQA2-like*AY312392- DQB2*AJ238946
#l	DRB1*GSF- DQA1*LN827890- DQB1*GU191460- DQA2*AY312387-DQA2-like*NullDQB2*HM367631
#m	DRB1*H3- DQA1*M33304- DQB1*HQ728667- DQA2-AY312377- DQA2-like*Null- DQB2LN868259
#o	DRB1*L- DQA1*LN736359- DQB1*AJ238945- DQA2*AY312389- DQA2-like*Null- DQB2*LN868258
#p	DRB1*M- DQA1*M33304-DQB1*GU191455 (GU191459)- DQA2*AY312382- DQA2-like*NullDQB2*Null

9.2.3 FEC

There have been previous detailed reports of FEC these animals (Bishop et al. 2004). It was measured on three occasions post weaning (**Table 46**). The transformation used was $\ln(\text{FEC} + 1)$. The transformation was used to remove skewness with 1 being added to avoid zero values and to correct for heterogeneity of variance and to produce approximately normally distributed data.

Table 46 The description of FEC in this study

Mean	July	August	September
Arithmetic	93	79	155
Geometric	17	22	41

9.2.4 Nematode Specific Plasma Antibodies Response

The IgE antibody activity serologic specific for L3 was analysed previously by Murphy et al. (2010) using indirect ELISA. The transformation used was $(\text{IgE} + 0.001)^{0.25}$ in order to normalise the IgE value.

9.2.5 Statistical Analysis

The significance of haplotype effect was determined in the **MIXED** model with overall F-test based on restricted maximum likelihood (REML) was applied to model which fitted year, date of birth, sex and nine haplotypes simultaneously (**Table 47**). Sire and dam were fitted as covariates. The most common haplotype, #p was set equal to zero in order to provide the best linear unbiased estimate of haplotype effects. The statistically significant haplotypes were identified by testing the p-values within the significance level of ($P < 0.05$). In the second model, haplotype homozygosity was fitted as fixed effect, together with year and date of birth.

9.3 Results

9.3.1 Association of MHC class IIa haplotypes and FEC

Figure 31 illustrates the association between haplotypes and FEC. Three haplotypes #ka, #a and #b had higher FEC; while, the rest of haplotypes were associated with lower FEC. The lowest FEC was observed in animals that had haplotype #d ($p < 0.05$, see **Table 47**).

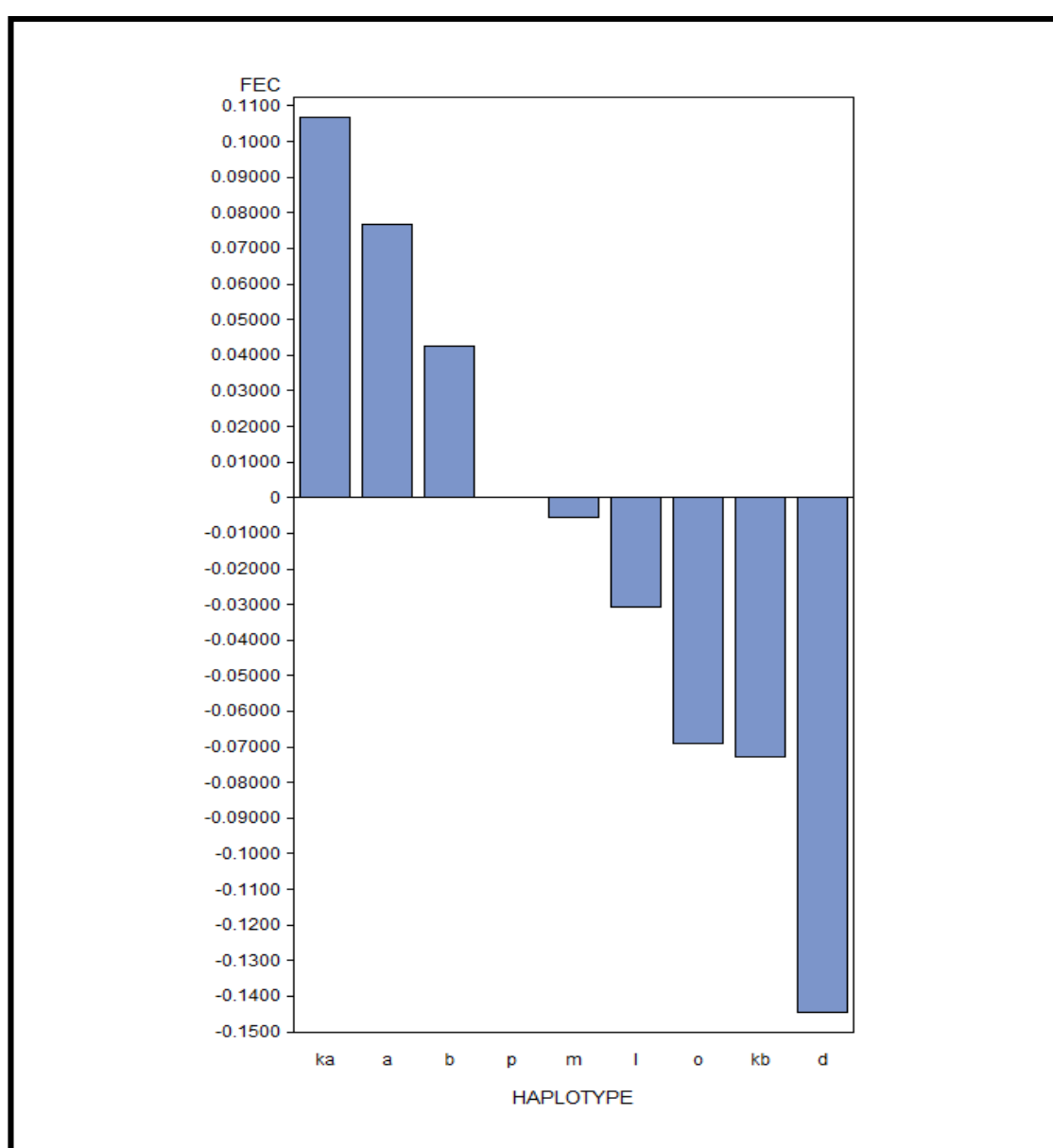


Figure 31 The association of the MHC class IIa haplotype with FEC. The most frequent haplotype, #p was set equal to zero and acted as a reference.

Table 47 The significance of effect of individual MHC class IIa haplotypes on FEC. See Table 46 for full haplotype MHC class IIa.

Effect	Num DF	Den DF	F value	Pr> F
Year	3	135	77.75	<0.001*
DOB	1	135	7.32	0.0077*
Sex	1	135	7.69	0.0063*
#a	1	135	0.87	0.3525
#b	1	135	0.14	0.7137
#d	1	135	5.52	0.0203*
#ka	1	135	3.04	0.0833
#kb	1	135	0.77	0.3831
#l	1	135	0.17	0.6811
#m	1	135	0.01	0.9300
#o	1	135	0.48	0.4876
#p	0	-	-	-

9.3.2 Association of MHC class IIa haplotypes and anti-L3 IgE

Figure 32 illustrates the association of haplotypes and IgE activities against L3. Two haplotypes, #a and #d have higher activity IgE against L3. The rest of haplotypes were associated with low IgE anti-L3. The lowest activity of anti-L3 IgE was observed in animals that possessed haplotype #l ($p < 0.05$, see **Table 48**).

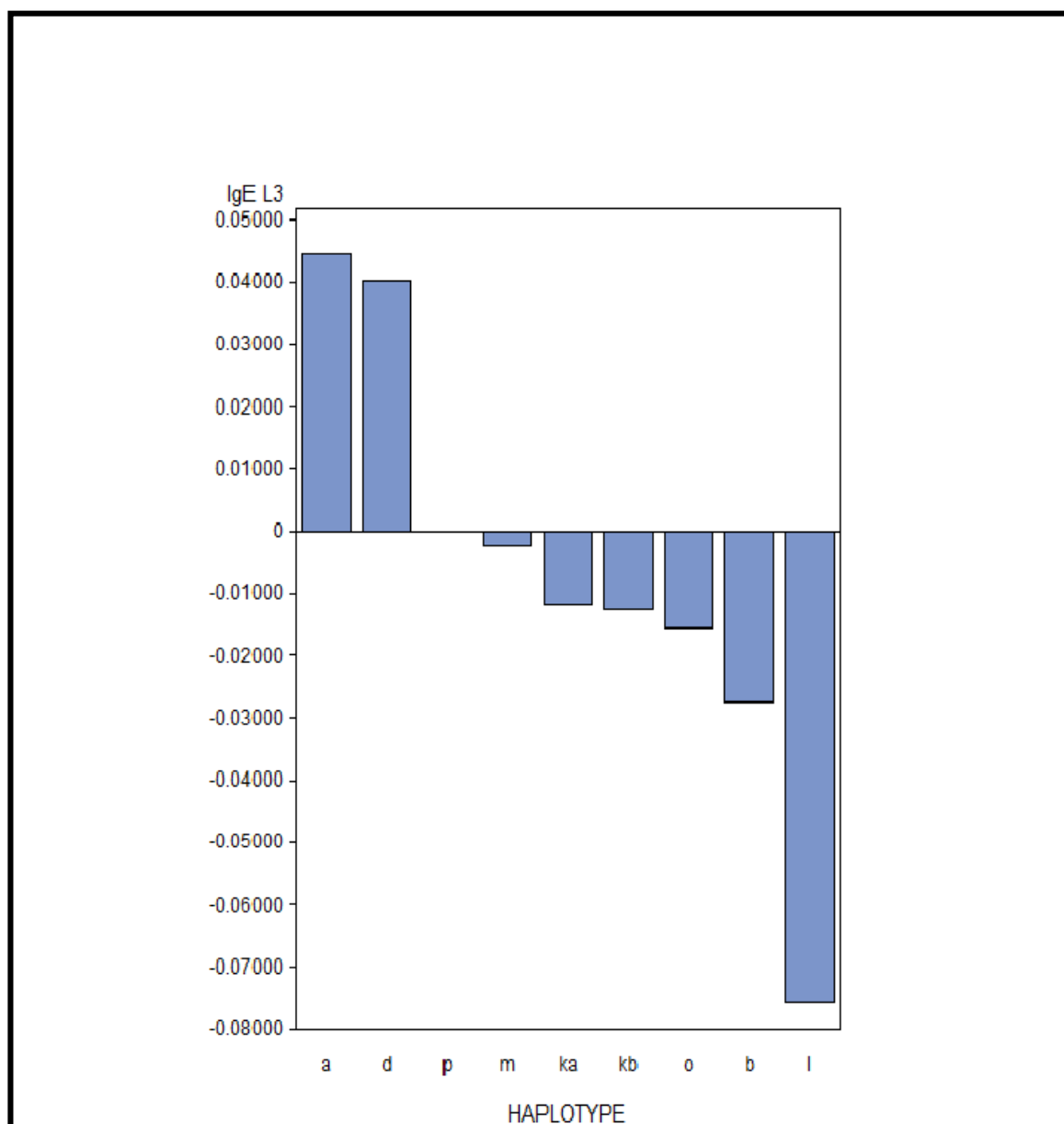


Figure 32 Association of the MHC class II haplotype with IgE activities against L3. The most frequent haplotype, #p was set equal to zero and acted as a reference.

Table 48 The significance of effect of individual MHC class IIa haplotype on anti-L3 IgE. The haplotype #p was set as a reference.

Haplotype	Num DF	Den DF	F value	Pr> F
Year	2	73	15.90	<0.01*
DOB	1	73	13.46	0.0005*
Sex	1	73	0.18	0.6695
#a	1	73	1.84	0.1796
#b	1	73	0.37	0.5436
#d	1	73	2.72	0.1031
#ka	1	73	0.22	0.6414
#kb	1	73	0.14	0.7065
#l	1	73	6.46	0.0132*
#m	1	73	0.01	0.9311
#o	1	73	0.15	0.7027
#p	0	0	-	-

9.3.3 Association of MHC class IIa homozygosity and nematode resistance

The effect of homozygosity on nematode resistance (FEC and anti-L3 IgE) is presented in **Table 49**. No significant associations were found between haplotype homozygosity and nematode resistance.

Table 49 The significance of effect of MHC class IIa homozygosity on FEC and anti-L3 IgE.

Variable	Num DF	Den DF	F value	Pr> F
FEC				
Year	2	92	52.34	0.0001*
DOB	1	92	7.17	0.0160*
Sex	1	92	7.11	0.0006*
homozygosity	1	92	5.74	0.7170
IgE activity against L3				
Year	2	92	52.34	0.0001*
DOB	1	92	7.17	0.0056*
Sex	1	92	7.11	0.7166
homozygosity	1	92	5.74	0.0965

9.4 Discussion

The aim of this chapter was to investigate the association between MHC class IIa haplotype and nematode resistance. Haplotype #d was significantly associated with low FEC. On the other hand, haplotype #l was significantly associated with low IgE activity against L3.

Association between MHC alleles and nematode resistance has been confirmed in sheep (Schwaiger et al. 1995; Paterson et al. 1998; Buitkamp & Epplen 2001; Charon et al. 2002; Sayers et al. 2005; Stear et al. 2005; Davies et al. 2006; Keane et al. 2005; 2007; Castillo et al. 2011; Valilou et al. 2015). Even though they have identified specific alleles being associated with resistance, but the true loci associated with nematode resistance still remain in question. The problem arose due to linkage disequilibrium (Stear et al. 2005). The previous chapters have provided evidence of strong linkage disequilibrium between MHC class IIa alleles in this Texel population (see **Chapter 8**). Therefore, haplotypic association with nematode resistance, instead of a single locus, has been duly addressed, in order to have a better understanding of mechanism of nematode resistance.

There are various methods of measuring nematode resistance in sheep. This includes parasitological, biochemical, haematological and immunological traits. In this study, two parameters of nematode resistance, FEC and anti-L3 IgE were used. The role of IgE in the nematode resistance process involves classical type I hypersensitivity reaction. Consequently, mucus production increases, hence blocking larval colonization and development leading to the rejection of the parasites (Pernthaner et al. 2005). The importance of IgE in nematode resistance is supported in experimental studies in sheep (Stear et al. 1995; Huntley et al. 2001; Hassan et al. 2011) and the result from Murphy et al. (2010) study indicate that the activity IgE is directed against protein molecules of L3 of nematode in resistant sheep.

The presence of association of MHC haplotype and nematode resistance or susceptibility in this flock verifies that combinations of certain alleles have its advantages and disadvantages (Kennedy 1989; Forrest et al. 2010). The difference among haplotypes on nematode resistance may be due to the different number of

parasite molecules recognised by the haplotype (Stear et al. 2007). In this context, in animals that possess haplotype #d, it would suggest that their MHC molecules are able to bind more parasite molecules and present it to T cells, consequently IgE is produced against more parasite molecules. Therefore, haplotype #d provides the best protection against nematodes. In contrast, sheep carrying haplotype #l, their MHC molecules were less able to bind to parasite molecules, less IgE production, and therefore, they were more susceptible to nematodes.

Schwaiger et al. (1995) revealed G2 as a resistant allele against nematodes in a Scottish Blackface population. However, in the present study, we revealed two different G2 haplotypes existed in this Texel population, #ka and #kb (**Table 46**). Both haplotypes have similar alleles except at DQB2 loci (present of AJ238935 or AJ238946 allele). One of G2 haplotype, #kb was associated with low FEC and another haplotype (#ka) was not. The evidence from the present study suggests that DQB2 locus plays an important role in the differences of nematode resistance status in sheep. Thus, this conclusion is consistent with previous investigation hypothesis that true resistant allele is in linkage disequilibrium with G2 (McCririe et al. 1997; Stear et al. 2005; Sayers et al. 2005; Keane et al. 2007; Hassan et al. 2011).

The importance of DRB1 locus cannot be ruled out when the data is compared with another breed. The haplotype #l in this study was associated with susceptibility against nematodes. The data from a Scottish Blackface flock revealed that the haplotype #G1 was associated with resistance (Stear et al. 2005). Interestingly, both haplotype #l and #G1 pose similar alleles except they differ at DRB1 locus. This advocates the vital role of DRB1 for the same disease. Given this, it is reasonable to propose that DRB1 and DQB2 together are important loci for determining the resistance against nematode in sheep.

Interestingly, Stear et al. (2005) has highlighted the effect of heterozygous advantage effect in MHC genes. A study of Blackface sheep has shown that heterozygous DRB1 animals were more resistant than homozygotes. In addition, the heterozygote advantage is a particularly appealing mechanism for explaining the IgE response to parasites, that leads to increased IgE concentrations (Lee et al. 2011). However, in this study, there was no evidence for a significant effect of heterozygosity at MHC class IIa haplotype on total FEC or IgE anti-L3.

9.5 Conclusion

In conclusion, the study has determined specific haplotypes in sheep that appear to be associated with nematode resistance or susceptibility. This finding supports the hypothesis that MHC plays a significant role in nematode resistance. It also contributes to the understanding of the mechanisms involved in nematode resistance in sheep.

CHAPTER 10

GENERAL DISCUSSION AND CONCLUSION

The aims of this thesis were outlined in chapter 1 and the relevant conclusions have been specified in respective chapters. This chapter will recap the significant findings emphasizing areas which require future research.

Gastrointestinal nematode infection remains a major constraint on production and welfare in domestic sheep in most geographical locations of the world, including in the UK. In addition, with the ever increasing occurrence of resistance to multiple classes of anthelmintic drugs, alternative methods of management, especially non-chemotherapeutic control is therefore much desired today.

Selective breeding for increased nematode resistance in sheep could offer a solution to this problem. This method has been proven successful in large livestock-producing countries such as Australia and New Zealand. In the UK, this approach has also been adopted in some commercial farms (Stear et al. 2007). FEC has been used widely as an indicator of nematode resistance in selective breeding. However, FEC has disadvantages as a marker, especially since it requires the animals to be infected with parasites.

Given this drawback, there is a clear need to search for alternative or better markers to identify and select resistant animals. Other phenotypic markers such as IgA level, pepsinogen concentration, and peripheral eosinophilia have been proposed as better markers for identifying resistant animals (Stear et al. 2009). Again, the markers require the animal to be infected with nematodes. In contrast, molecular or genetic markers might be good candidates because they can allow selection at younger ages and does not require the animal to be infected with parasites.

The association between molecular markers and resistant phenotypes has been studied. One of the potential molecular markers of nematode resistance is MHC. MHC genes encoding the MHC molecules, which is the glycoprotein present on the surface of cells. MHC molecules are responsible for presenting antigen peptides and induction of

adaptive immunological responses. Therefore, MHC is a core component in the vertebrate immune system.

There is a body of scientific literature linking MHC class II and the ability of animals to resist infection by GIN. Associations between MHC class II and resistance to nematode infection have been confirmed in cattle, mice, guinea pigs and pigs (Stear & Murray 1994). In sheep, the associations between polymorphism of MHC genes and nematode resistance have been established. This association is observed in various breeds, which include Suffolk (Sayers et al. 2005), Scottish Blackface (Schwaiger et al. 1995), Pelibuey (Castillo et al. 2011) and Ghezel (Valilou et al. 2015). Therefore, MHC class II genes are considered among the most important genes for controlling nematode resistance. In order to confirm the importance of MHC in mechanism of resistance, this thesis has performed investigations to characterise MHC class II genes, and also to establish the role of the MHC genes in nematode resistance specifically in Texel population.

Basically, this study has succeeded in achieving five main goals:

1. The establishment of a sequence-based typing system for MHC Class IIa genes.
2. The characterization of the Ovar-MHC class IIa diversity profile in Texel population.
3. The establishment of haplotype and extent of linkage disequilibrium in Texel population.
4. The detection of novel association between MHC haplotypes and nematode resistance.
5. The investigation of evolutionary history of MHC class II genes.

1. Establishment of sequence-based typing system

MHC genes are a highly complex system in vertebrate genome due to extreme polymorphism. They are known to be the most polymorphic genes in the human genome. Due to this nature, typing of MHC genes is a daunting and challenging task. In

the past, a range of typing methods have been developed from serological and cellular typing, now molecular approaches offer several advantages.

Sequence-based typing, based on DNA, is widely used in humans and animals. This technique is a high-resolution system recommended for the study of MHC diversity in large sheep populations (Ballingall & Tassi, 2010). The basic steps involved in sequence-based typing include PCR amplification of specific coding regions of MHC genes and sequence of the amplified amplicon. The advantage of this method compared to other techniques is due to its ability to capture the polymorphisms efficiently, amplify all alleles and provide high quality sequence output (Ballingall & Tassi, 2010).

In sheep, the technique has only been applied in highly expressed DRB1 locus (Sayers et al. 2005b; Ballingall & Tassi, 2010). To our knowledge, the sequence-based typing has yet to be applied in DQA or DQB loci in sheep. Therefore, in this study, we have successfully developed a sequence-based typing not only for DRB1 gene, but also for DQA1, DQA2, DQB1 and DQB2 genes in sheep.

Sequence-based typing depends on reliable primers that can capture all variant of alleles (Ballingall & Tassi, 2010). Primer binding site polymorphism leads to failure of amplification of certain alleles due to mismatch in distinct position of the primer sequence or the annealing failure in binding sites. In this study, except at DQA2 locus, at least two primer sets were used for typing of locus. The use of additional primers not only serves to validate the homozygous animal, it also validates the allele assignment from the first primer (Ballingall & Tassi, 2010). Surprisingly, four primer sets were required to enable to capture all variants at DQA1 locus in Texel population. These include two allele-specific primers for detection of specific DQA1 alleles.

The other challenge encountered in MHC typing is different MHC loci can possess a high degree of similarity between sequences, resulting from recombination and gene conversion events. However, in this study, a locus by locus approach seems to be effective for characterising MHC class II genes in the Texel population. It should be noted that with DQB1 locus (Chapter 6), locus assignment encountered only minor problems because the primer set amplified three sequences from single animal. This problem was resolved by use of another set of primers. The findings from this study emphasized the value of multiple primers in sequence-based typing for establishing

the MHC alleles in each population. Generally, sequence-based typing system through locus by locus approach has been successfully developed in this study. The development of this technique would enable other investigators to determine the variation of MHC class II in other population.

2. The characterization of the Ovar-MHC class IIa profile in Texel population

MHC diversity in population has always been of great interest to biologists and ecologists. This thesis has also enhanced previous MHC research, by characterising genetic diversity at the nucleotide and amino acid levels. The accurate determination of the allelic diversity pattern and the structural sequence variation is essential for understanding the functional importance of MHC diversity.

In chapter 3, Ovar-DRB1 exhibited a high degree of variation. Texel population in this study comprised 18 DRB1 alleles. This number is higher compared too only eight DRB1 alleles detected by Sayers et al. (2005b) study in the same breed. This indicates that identifying MHC allelic diversity requires the testing of large numbers of sheep.

In chapters 4 and 5, the diversities of DQA1 and DQA2 genes were determined. The DQA2 (including DQA2-like) has slightly higher number of alleles compared to DQA1 loci (eight and nine alleles respectively). Eight novel alleles were discovered from the amplification of DQA1 gene and have been submitted to the database. The work detailed in these two chapters extends and confirms previous descriptions of the polymorphism of DQA1 and DQA2.

In chapters 6 and 7, the diversity of DQB1 and DQB2 genes were described. In total, 13 DQB1 and 16 DQB2 sequences were obtained. This makes DQB2 the second diverse locus among MHC class IIa, after DRB1 locus. Six novel DQB alleles were identified and submitted to the database. Within this four chapters (Chapter 4, 5, 6 and 7), allelic frequencies of DQA1, DQA2, DQB1 and DQB2 were also individually estimated and it was revealed that the allelic frequencies vary. This allelic diversity information is valuable for the purpose of comparison with other populations.

Class II molecules are formed by alpha and beta chains encoded by genes within the MHC class II. These molecules form the peptide-binding site that has many

polymorphic sites (Brown et al. 1993) and this site is responsible for binding and presenting peptides to CD4⁺ T lymphocytes. This peptide-binding site is encoded by the exon 2 of Class II DR and DQ genes. In this study, diversity in the predicted amino acid sequences of the MHC class II alleles were observed at positions which are considered to be important as antigen binding sites. Diverse amino acids at these positions may impact the specificity of the antigen binding sites thus affecting the peptide binding ability (Bondinas et al. 2007). The x-ray crystal study structure of DR and DQ molecules in sheep or other closely related species in the future would be helpful in understanding the MHC molecule binding site in sheep.

3. The determination of haplotype and extent of linkage disequilibrium in Texel flock

Haplotype is defined as a combination of alleles at different sites along the same chromosome that are transmitted as one unit (Crawford & Nickerson 2005). Haplotype study can mark recombination process, and this knowledge of recombination is essential to identify the disease-causing locus (Crawford & Nickerson 2005). In Chapter 8, Texel MHC class IIa haplotype profiles were firmly established. The haplotypes were directly determined from pedigrees. One advantage in animal study is that several generations can be made available in a single study, like the samples in this population. The basic principle of the pedigree method relies on the fact that haplotype will be inherited as a unit unless they are separated by a recombination event.

This study enabled the identification of only 21 haplotypes in our Texel population, which illustrates non-random association of alleles. No recombination was observed at any of the MHC class IIa loci. In addition, haplotype determination has also revealed that there is variation in the number of DQ genes per haplotypes. The variable number of DQ genes is in line with a report in cattle (Ballingall et al. 1997; Sigurdardottir et al. 1998). It was suggested that gene duplication or deletion among MHC genes is responsible for inconsistency in the number of DQ genes in cattle (Sigurdardottir et al. 1992).

Linkage disequilibrium is the non-random association of alleles at different loci (Slatkin 2008). Linkage disequilibrium pattern is now a growing area of interest in genetic studies because the information would assist in fine mapping of complex trait

genes. In addition, patterns of linkage disequilibrium also aid the understanding of biological and demographic processes such as mutation, recombination, population history and selection (Slatkin 2008). Stear et al. (2007) suggest that the investigation of linkage disequilibrium pattern between breeds provides an opportunity to disentangle the effects of alleles at closely linked loci in defining a true resistance allele for nematode resistance.

In Chapter 8 also, the extent of linkage disequilibrium among MHC class IIa was determined. Two parameters of linkage disequilibrium; r and D' have been reported in this study. Obviously, two different measures give different interpretation. The result also shows there was strong linkage disequilibrium observed between specific loci. The finding of strong linkage disequilibrium between loci emphasized the use of haplotype in defining association between MHC and nematode resistance, which is the main objective of this thesis.

4. The detection of novel association between MHC class II haplotypes and nematode resistance

The associations between MHC class II genes and resistance to nematode infection in sheep have been observed in many studies involving multiple breeds (Schwaiger et al. 1995; Paterson et al. 1998; Buitkamp & Epplen 2001; Charon et al. 2002; Sayers et al. 2005; Stear et al. 2005; Davies et al. 2006; Keane et al. 2005; 2007; Castillo et al. 2011; Valilou et al. 2015). Even though a specific allele was found to be associated with nematode resistance, the concern is that there is a possibility of an other locus or loci that linkage disequilibrium which could be a 'true player' in nematode resistance (Schwaiger et al. 1995; Keane et al. 2007). This concern arose due to absence of an association between MHC and FEC in some sheep population (Blattman et al. 1993; Sayers et al. 2005b).

In chapter 9, haplotype association with nematode resistance, instead of single gene was investigated in Texel population. Haplotype association is recommended due to strong linkage disequilibrium nature in MHC genes (Hassan et al. 2011). The association of MHC haplotype and resistance to GIN, was measured using two indicators of nematode resistant namely FEC and IgE anti-L3 activity. There were significant associations between two specific haplotypes and nematode resistance. The

haplotype #d had a significant effect on the resistance against GIN. In contrast, the haplotype #l is significantly associated with susceptibility against the GIN. This indicates that the specific MHC haplotype can provide protection against nematodes in this population. The resistance haplotype in this Texel maybe possess essential amino acids which facilitate an effective immuneresponse (Sayers et al. 2005b; Stear et al. 2009).

5. The investigation the evolutionary history of MHC class II genes

The evolutionary history of MHC Class IIa genes were revealed through phylogenetic neighbour-joining trees. Some of these trees revealed the similarities between the sheep, cattle and caprine sequences. The reason for this similarity, as suggested earlier by many authors, is due to pathogens which provide selection pressure to keep specific MHC alleles which are necessary to mount an effective immune response (Zhou & Hickford, 2004). These alleles predate speciation according to the trans-species hypothesis (Klein, 1987) who argued that over evolutionary time a group of ancestral alleles were passed on to a species descendants.

Even though the Texel sample in this study was limited in size, it provides evidence that the MHC genes could be used as genetic marker in selective breeding programs. This study highlights a particular MHC haplotype responsible for nematode resistance and susceptibility against nematodes. However, this study does not provide a clear picture of the mechanism underlying nematode resistance. There is clearly a need for further research to determine the causative mutation of nematode resistance, for example, to define SNP associated with the resistance. In addition, an association between MHC haplotypes and a set of parasite epitopes would certainly be another option to widen knowledge of the molecular networks involved in nematode resistance. Although the association between MHC and GIN resistance have been established, it is still limited in certain countries and breeds. The association should be addressed in less developed countries in the future.

Conclusion

In conclusion, the work in this thesis has extended further our knowledge about a host/parasite relationship, which has always been very complex. The genetic diversity of the MHC class IIa and their relationship with nematode resistance has been confirmed in Texel population. It can be concluded that the MHC genes play an important role in development of resistance against GIN in Texel population.

LIST OF APPENDICES

Appendix 1: Pedigree Record

lamb	Year	Sire	Dam
100t001	9077	9t077	8y014
100t004	9027	9y027	8y005
100t006	9026	9y026	8y012
100t009	9077	9t077	8t047
100t011	9027	9y027	8y013
100t012	9027	9y027	8y013
100t013	8055	8t055	8t008
100t014	9026	9y026	8t018
100t016	9027	9y027	8t074
100t018	9027	9y027	8y019
100t020	9077	9t077	7t035
100t021	9077	9t077	7t035
100t022	8055	8t055	7t064
100t023	8055	8t055	7t064
100t025	9027	9y027	8t046
100t026	9077	9y025	8t038
100t027	9025	9y025	8t038
100t029	9060	9t060	6y172
100t030	9027	9y027	8y009
100t031	9027	9y027	8y009
100t032	8055	8t055	6y154
100t033	8055	8t055	6y154
100t034	8055	8t055	6y154
100t038	9026	9y026	9y024
100t039	9077	9t077	9y003
100t041	8055	8t055	7t028
100t042	9026	9y026	7t012
100t045	9027	9y027	8y001
100t046	9027	9y027	8y001
100t048	9025	9y025	8y003
100t050	9026	9y026	9y001
100t051	9026	9y026	9y001
100t053	9026	9y026	8y004
100t055	9025	9y025	8y011
100t059	9025	9y025	8t020

100t060	9025	9y025	8t020
100t062	8055	8t055	9y013
100t063	9060	9t060	8t013
100t065	9027	9y027	8t058
100t066	9077	9t077	6y156
100t067	9027	9y027	6y174
100t068	9027	9y027	6y174
100t069	9027	9y027	6y174
100t070	9026	9y026	7t034
100t073	8055	8t055	8y002
100t078	9043	9t043	7t029
100t079	9043	9t043	7t029
100t080	9043	9t043	7t029
100t082	9026	9y026	6y175
100t083	9026	9y026	6y175
100t084	9027	9y027	9y010
100t085	9027	9y027	9y010
100t086	9027	9y027	6y170
100t087	9027	9y027	6y170
100t088	8055	8t055	8t026
100t089	9026	9y026	8y006
100t094	9026	9y026	6y178
100t097	9026	9y026	9y035
100t100	9025	9y025	8t012
100t101	9025	9y025	8t012
100t104	9025	9y025	8t073
100t105	9025	9y025	8t073
100t107	9025	9y025	8t009
100t108	9025	9y025	8t040
100t114	8055	8t055	8t015
100t115	8055	8t055	8t015
100t116	9043	9t043	4p428
100t119	8055	8t055	8y010
100t121	9043	9t043	9y004
100t127	9026	9y026	6y158
100t128	9026	9y026	6y158

100t130	8055	8t055	9y008
100t132	9025	9y025	8y016
100t136	9026	9y026	8t043
100t137	8055	8t055	3p412
100t142	8055	8t055	6y164
100t145	9060	9t060	6y165
100t146	9060	9t060	9y011
100t147	9026	9y026	9y011
100t149	9025	9y025	8y015
100t154	9025	9y025	3p411
100t155	?	.	9y030
100t157	?	.	9y015
100t158	?	.	8t045
100t159	?	.	8t045
100t160	9027	9y027	4p444
100t161	9027	9y027	4p444
100t162	9025	9y025	6y160
100t163	9025	9y025	9y034
100t164	9025	9y025	9y034
100t166	9025	9y025	4p447
100t167	9025	9y025	4p447
100t168	9025	9y025	9y014
100t169	9025	9y025	9y014
100t171	9025	9y025	8t023
100t172	9025	9y025	6y162
100t173	9025	9y025	9y032
100t175	9025	9y025	8t027
100t176	9025	9y025	8t027
100t179	9025	9y025	9y023
098t001	7070	7t070	6y168
098t002	7026	7t026	2p437
098t003	7026	7t026	2p437
098t004	7070	7t070	6y173
098t005	7070	7t070	6y173
098t006	7051	7t051	7y001
098t009	7026	7t026	1p413
098t010	7051	7t051	4p446
098t011	7051	7t051	4p446
098t012	7058	7t058	3p409
098t013	7051	7t051	4p444
098t014	7058	7t058	3p411
098t015	7058	7t058	3p417

098t016	7058	7t058	3p417
098t017	7058	7t058	4p425
098t018	7051	7t051	4p439
098t020	7070	7t070	4p403
098t021	7070	7t070	4p403
098t022	7026	7t026	6y172
098t023	7026	7t026	4p448
098t024	7070	7t070	6y167
098t025	7070	7t070	6y167
098t026	7051	7t051	4p418
098t027	7051	7t051	4p418
098t028	7070	7t070	6y158
098t030	7051	7t051	4p434
098t031	7026	7t026	4p432
098t032	7026	7t026	4p432
098t033	7026	7t026	6y176
098t034	7026	7t026	6y176
098t035	7026	7t026	4p409
098t036	7026	7t026	4p409
098t037	7026	7t026	6y154
098t038	7070	7t070	6y170
098t039	7026	7t026	4p438
098t040	7026	7t026	4p438
098t041	7070	7t070	6y174
098t042	7070	7t070	6y174
098t043	7070	7t070	6y157
098t044	7070	7t070	6y157
098t045	7026	7t026	4p437
098t046	7026	7t026	4p428
098t047	7026	7t026	4p428
098t048	7070	7t070	7y161
098t049	7070	7t070	7y161
098t050	7163	7y163	2p410
098t051	7163	7y163	2p410
098t052	7163	7y163	7y162
098t053	7163	7y163	6y164
098t054	7163	7y163	6y180
098t055	7163	7y163	6y178
098t056	7026	7t026	3p426
098t057	7026	7t026	3p426
098t058	7070	7t070	6y165
098t059	7070	7t070	6y165

098t060	7163	7y163	3p412
098t061	7070	7t070	6y161
098t062	7163	7y163	6y156
098t063	7163	7y163	6y156
098t064	7163	7y163	6y162
098t068	7026	7t026	6y160
098t070	7163	7y163	6y169
098t072	7163	7y163	4p424
098t073	7163	7y163	7y002
098t074	7163	7y163	7y002
099t005	8053	8t053	8y013
099t007	8053	8t053	7y162
099t008	8053	8t053	7y162
099t009	8022	8t022	8y014
099t016	8053	8t053	8y017
099t017	8053	8t053	8y017
099t019	8070	8t070	8y018
099t020	8022	8t022	4p448
099t021	8022	8t022	4p448
099t022	8061	8t061	8y006
099t024	8053	8t053	7t025
099t026	8022	8t022	6y170
099t027	8022	8t022	3p412
099t028	8053	8t053	8y002
099t029	8061	8t061	8y002
099t031	8070	8t070	6y175
099t035	8022	8t022	8y004
099t036	8061	8t061	4p409
099t037	8053	8t053	6y172
099t040	8070	8t070	4p403
099t042	8053	8t053	6y154
099t043	8070	8t070	6y165
099t044	8022	8t022	6y174
099t046	8061	8t061	7t037
099t048	8070	8t070	6y167
099t049	8070	8t070	6y167
099t050	8053	8t053	3p411
099t051	8070	8t070	8y008
099t053	8053	8t053	6y158
099t054	8053	8t053	7t036
099t055	8053	8t053	4p437
099t056	8053	8t053	4p437

099t057	8053	8t053	7t064
099t058	8053	8t053	7t029
099t059	8053	8t053	7t029
099t060	8053	8t053	6y178
099t061	8053	8t053	6y178
099t062	8070	8t070	4p428
099t064	8061	8t061	4p444
099t065	8061	8t061	4p444
099t066	8070	8t070	6y156
099t067	8070	8t070	6y156
099t069	8053	8t053	6y169
099t071	8022	8t022	7t034
099t072	8007	8y007	6y159
099t073	8007	8y007	6y159
099t074	8007	8y007	8y003
099t075	8070	8t070	8y019
099t076	8070	8t070	8Y019
099t077	8007	8y007	8y011
099t079	8061	8t061	6y157
099t080	8022	8t022	6y168
099t081	8022	8t022	6y168
099t082	8053	8t053	4p447
099t083	8053	8t053	4p447
099t085	8053	8t053	4p434
099t086	8007	8y007	6y173
099t087	8007	8y007	6y173
099t088	8061	8t061	8y015
099t091	8007	8y007	4p425
099t092	8007	8y007	6y160
099t093	8007	8y007	4p425
099t094	8007	8y007	7t012
099t096	8007	8y007	6y180
099t097	8007	8y007	7t028
7t051	7051	.	.
7t058	7058	.	.
7t070	7070	.	.
7y163	7163	.	.
8y007	8007	.	.
9y025	9025	.	.
9y026	9026	.	.
9y027	9027	.	.

Appendix 2: Solution and Media Preparation

1M Tris-HCl pH7.5

A 121g Trizma base (Tris [hydroxymethyl] aminomethane; Sigma-Aldrich Company Ltd, Poole, England), was weighed and dissolved in 800 ml distilled water (dH₂O) and the pH was adjusted to 7.5 using Microprocessor pH meter (HANNA Instrument). The volume was adjusted to 1 litre and the solution stored at 4°C.

1M MgCl₂

A 203.3g MgCl₂.6H₂O (BDH Chemicals Ltd, Poole, England), was weighed and dissolved in 800 ml dH₂O. The volume was adjusted to 1L and autoclaved. The solution was stored at 4°C.

5M NaCl₂

292.2g NaCl (Sigma- Aldrich) was weighed and dissolved in 800ml dH₂O. The volume made up to 1L, autoclaved and stored at 4°C.

0.5M EDTA pH8.0

A 93.05g EDTA (Ethylene Diamine Tetra Acetic Acid- Sigma-Aldrich) was weighed and made up to 500 ml in dH₂O and the pH was adjusted to 8.0, autoclaved and afterward stored at 4°C.

10% SDS pH7.2

A 100g SDS (Sodium Dodecyl Sulfate, Sigma Aldrich) was weighed and mixed with 800 ml dH₂O. The solution was heated to dissolve the SDS, and then the pH adjusted to 7.2. The volume was made up to 1 litre and stored at room temperature.

Proteinase K

100 mg proteinase K (Sigma-Aldrich) was dissolved in 25 ml dH₂O to make a 4 mg proteinase K/ml. 500 µl of this solution was mixed with 500 µl 10% SDS

3M Sodium Acetate pH5.2

A 204.1g NaAc.3H₂O (BDH-Limited) was mixed with 350 ml dH₂O and the pH was adjusted to 5.2 with Glacial Acetic Acid. The volume was adjusted to 500 ml dH₂O, autoclaved and stored at 4°C.

TE Buffer

A 2ml 0.5M EDTA and 10 ml 1.0M Tris-HCl was mixed with dH₂O and made up to 1L. The solution was autoclaved and stored at 4°C.

Chloroform: Isoamylalcohol (24:1)

240 ml chloroform (Sigma-Aldrich) was mixed with 10 ml isoamylalcohol (Sigma-Aldrich) and stored at 4°C.

Lysis Buffer

A 109.536g Sucrose (Sigma-Aldrich) was dissolved in 10 ml 1M Tris-HCl pH7.5 and 5 ml 1M MgCl₂ to make up 990ml with dH₂O. The solution was then autoclaved and 10ml of 10% Triton × 100 (Sigma-Aldrich) was added and the buffer was stored at 4°C.

Digestion Buffer

7.5ml 5M NaCl₂ and 25 ml 0.5M EDTA (pH8.0) was mixed with dH₂O to make up 500 ml. The solution was autoclaved and stored at 4°C.

LB medium

In a 500ml bottle (plastic top) 5g tryptone, 2.5g yeast extract (Oxoid Ltd., Basingstoke, Hampshire, England) and 2.5g NaCl (Sigma-Aldrich Ltd., UK) were added to dH₂O, made up to 490 ml with dH₂O, pH adjusted to 7 with NaOH, then made up to final volume of 500ml – autoclave.

LB plates

7.5g of agar (Oxoid Ltd., Basingstoke, Hampshire, England) were added to a 500ml bottle of LB – autoclave and allow the medium to cool to around 55°C, then add 500ul ampicillin (final conc. 100µg/ml) and 500ul X-Gal (final conc. 50µg/ml).

TOPO® Cloning Reaction

The PCR products were TOPO® cloned into the One Shot®Mach1™-T1R CompetantCells (chemically competent E. coli cells) were transformed with the recombinant vector according to the manufacturer's instruction.

Appendix 3: Master Mix Preparation for PCR reactions

3.1 Ovar-DRB1

Primer ERB3/ SRB3 and DRB1_27F/ DRB1_27R

Reagents	Master Mix		
	1	12	20
Sterile water	13.3	160	266
10X Buffer	2.5	30	50
MgCl ₂	1.5	18	30
Primer F	0.5	16	10
Primer R	0.5	6	10
dNTP	0.5	6	10
Taq	0.2	6	4

3.2 Ovar-DQA1

Primer NikDQA1F/NikDQA1R, DQA1_92.y085F/ DQA1_92.y085R and DQA1_Z28518F/DQA1_Z28518R

Reagents	Master Mix		
	1	20	30
Sterile water	15.3	306	459
10X Buffer	2.0	40	60
Primer F	0.5	10	15
Primer R	0.5	10	15
dNTP	0.5	10	15
Taq	0.2	4	6

3.3 Ovar-DQA2

Primer: DQA2_F /DQA2_R

Reagents	Master Mix		
	1	20	30
Sterile water	17.0	340	510
10X Buffer	2.0	40	60
Primer F	0.25	5	7.5
Primer R	0.25	5	7.5
dNTP	0.5	10	15
Taq	0.2	4	6

3.4 Ovar-DQB1

Primer: JM05/ JM06

Reagents	Master Mix	
	1	26
Sterile water	12.8	333
10X Buffer	2.0	52
MgCl ₂	1.5	39
Primer F	0.5	13
Primer R	0.5	12
dNTP	0.5	13
Taq	0.2	5.2

Primer: 991/ 994

Reagents	Master Mix (2222)	
	1	26
Sterile water	13.8	358
10X Buffer	2.0	52
MgCl ₂	1.5	39
Primer F	0.5	13
Primer R	0.5	12
dNTP	0.5	13
Taq	0.2	5.2

3.5 Ovar-DQB2 :Primer: JM05/JM07; 1005/1007 and MJS05/JM07

Reagents	Master Mix	
	1	20
Sterile water	12.3	246
10X Buffer	2.5	50
MgCl ₂	1.5	30
Primer F	0.5	10
Primer R	0.5	10
dNTP	0.5	10
Taq	0.2	4.0

Appendix 4: MHC Class II Database

4.1 DRB1

Sheep

>ENA|AB017204|AB017204.1 Ovis aries Ovar-DRB1*0801 gene for DR beta-chain antigen binding domain, partial cds.
GGAGTATTATAGGAGCGAGTGTCAATTTCTTCAACGGGACCGAGAGGGTGCGGCTCCTGGAAAGATACTTCCAT
AATGGAGAAGAGTTTCGCGCGCTTCGACAGTGAAGTGGGGCGAGTTTCGGGCAGTGACCGAGCTGGGGAGGCCGG
CCGCTGAGCAATGGAACAGCCAGAAGAATCCTGGAGCAGAAGCGGGCCGAGGTGAACACGGTGTGCAGACA
CAACTATGGGGTCTTTGA

>ENA|AB017205|AB017205.1 Ovis aries Ovar-DRB1*0201 gene for DR beta-chain antigen binding domain, partial cds.
GGAGTATTCTACGAGCGAGTGTCAATTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGATCCT
GGAGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCATTGA

>ENA|AB017206|AB017206.1 Ovis aries Ovar-DRB1*0203 gene for DR beta-chain antigen binding domain, partial cds.
GGAGTATTCTACGAGCGAGTGTCAATTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGA
CAGATACTTCTATAATGGAGAAGAGACCTGCGCTTCGACAGCGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGATCCT
GGAGCGGAAGCGGGCCCGCTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGA

>ENA|AB017207|AB017207.1 Ovis aries Ovar-DRB1*03012 gene for DR beta-chain antigen binding domain, partial cds.
GGAGTATCATAAGAGCGAGTGTCAATTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGA
CAGATACTTTCTATAATGGAGAAGAATTCGTGCGCTTCGACAGCGACTGGGGCGAGTTCCG
GGCGGTGGCCGAGCTGGGGCGGCCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGCTCCT
GGAGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCTTTGA

>ENA|AB017208|AB017208.1 Ovis aries Ovar-DRB1*0404 gene for DR beta-chain antigen binding domain, partial cds.
GGAGTATGCTAAGAGCGAGTGTCTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGA
AAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGACTTCCT
GGAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACCTACGGGGTCATTGA

>ENA|AB017209|AB017209.1 Ovis aries Ovar-DRB1*0109 gene for DR beta-chain antigen binding domain, partial cds.
GGAGTATACTAAGAAAGAGTGTCTTTCTTCAACGGGACGGAGCGGGTGCGGTACCTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGCTCCT
GGAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGA

>ENA|AB017210|AB017210.1 Ovis aries Ovar-DRB1*1202 gene for DR beta-chain antigen binding domain, partial cds.
GGAGTATACTAAGAAAGAGTGTCAATTTCTTCAACGGGACGGAGCGGGTGCGGTTGCTGGA
AAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCG
GGCGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGATTTCTC
GGAGAGCAGGAGGACCGCGGTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGA

>ENA|AB017211|AB017211.1 Ovis aries Ovar-DRB1*0703 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATAGTAAGAGCGAGTGTTCATTTCTTCAACGGGACCGAGCGGGTGCGGTTTCCTGGA
CAGATACTACACTAACGGAGAAGAGAACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCG
GGCGGTGACCGAGCTGGGGCGGCCGGACGCTGAGCAATGGAACAGCCAGAAGGACTTCCT
GGAGAGCAGGAGGACCGCGGTGGACACGTACTGCAGACACAACCTACGGGGTTCGGTGA

>ENA|AB017212|AB017212.1 *Ovis aries* Ovar-DRB1*0702 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATAGTAAGAGCGAGTGTTCATTTCTTCAACGGGACCGAGCGGGTGCGGTTTCCTGGA
CAGATACTACACTAACGGAGAAGAGAACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCG
GGCGGTGACCGAGCTGGGGCGGCCGGACGCTGAGCAATGGAACAGCCAGAAGGACTTCCT
GGAGAGCAGGAGGACCGCGGTGGACACGTACTGCAGACACAACCTACGGGGTTCCTTGA

>ENA|AB017213|AB017213.1 *Ovis aries* Ovar-DRB1*1201 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATACTAAGAAAGAGTGTTCATTTCTTCAATGGGACGGAGCGGGTGCGGTTGCTGGA
AAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCG
GGCGGTGGCCGAGCTGGGGCGGCCGGAAGCCAAGTACTGGAACAGCCAGAAGGAGATCCT
GGAGAGCAGGAGGACCGCGGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB017214|AB017214.1 *Ovis aries* Ovar-DRB1*0323 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATCATAAGAGCGAGTGTCTGTTTCTTCAACGGGACCGAGCGGGTGCGGTACCTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGAGCGCCGAGTACTGGAACAGCCAGAAGGACTTCCT
GGAGCAGACGCGGGCCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB017215|AB017215.1 *Ovis aries* Ovar-DRB1*0333 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATCATAAGAGCGAGTGTCTGTTTCTTCAACGGGACCGAGCGGGTGCGGTACCTGGA
CAGATACTTCCATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGAGCGCCGAGTACTGGAACAGCCAGAAGGACTTCCT
GGAGCAGACGCGGGCCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB017216|AB017216.1 *Ovis aries* Ovar-DRB1*1101 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATGCTAAGAGCGAGTGTTCATTTCTTCAACGGGACCGAGCGGGTGCGGTTTCCTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCG
GGCGGTGGCCGAGCTGGGGCGGCCGGAGCGCCGAGTACTGGAACAGCCAGAAGGACTTCCT
GGAGCAGACGCGGGCCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTTCGGTGA

>ENA|AB017217|AB017217.1 *Ovis aries* Ovar-DRB1*1001 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATACCAAGAAAGAGTGTTCATTTCTTCAACGGGACCGAGCGGGTGCGGTTTCCTGGA
CAGATACTTCCATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGATCCT
GGAGCAGACGCGGGCCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB017218|AB017218.1 *Ovis aries* Ovar-DRB1*03411 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATCATAAGAGCGAGTGTTCATTTCTTCAACGGGACCGAGCGGGTGCGGTTTCCTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCG
GGCGGTGGCCGAGCTGGGGCGGCCGGAAGCCAAGTACTGGAACAGCCAGAAGGAGATCCT
GGAGCGGAAGCGGGCCGCCGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB017219|AB017219.1 *Ovis aries* Ovar-DRB1*03412 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATCATAAGAGCGAGTGTTCATTTCTTCAACGGGACCGAGCGGGTGCGGTTTCCTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCG
AGCGGTGGCCGAGCTGGGGCGGCCGGAAGCCAAGTACTGGAACAGCCAGAAGGAGATCCT
GGAGCGGAAGCGGGCCGCCGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB017220|AB017220.1 *Ovis aries* Ovar-DRB1*0352 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATCATAAGAGCGAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTTCCTGGA
CAGATACTTCCATAATGGAGAAGAGTTTCGTGCGCTTCGACAGCGACTGGGGCGAGTTCCG
GGCGGTGGCCGAGCTGGGGCGGCCGGACGCCGAGTACTGGAACAGCCAGAAGGAGCTCCT
GGAGCGGAGACGGACCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCTTTGA

>ENA|AB017221|AB017221.1 Ovis aries Ovar-DRB1*0605 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATCGTAAGAGCGAGTGTTCGTTTCTTCAACGGGACGGAGCGGGTGCGGTACCTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGCTCCT
GGAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACCTACGGGGTTCGGTGA

>ENA|AB017222|AB017222.1 Ovis aries Ovar-DRB1*0602 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATCGTAAGAGCGAGTGTTCGTTTCTTCAACGGGACGGAGCGGGTGCGGTACCTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGCTCCT
GGAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACCTACGGGGTTCGGTGA

>ENA|AB017223|AB017223.1 Ovis aries Ovar-DRB1*0603 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATCGTAAGAGCGAGTGTTCGTTTCTTCAACGGGACGGAGCGGGTGCGGTACCTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGAGCGCCGAGTACTGGAACAGCCAGGAGGAGCTCCT
GGAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACCTACGGGGTTCGGTGA

>ENA|AB017224|AB017224.1 Ovis aries Ovar-DRB1*1301 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATTCTACGAGCGAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTGCTGGA
CAGATACTTCCATAATGGAGAAGAGTTTCGTGCGCTTCGACAGCGACTGGGGCGAGTTCCG
GGCGGTGGCCGAGCTGGGGCGGCCGGAGCGCCGAGTATTGGAACAGCCAGAAGGACTTCCT
GGAGAGCAGGAGGACCGCGGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB017225|AB017225.1 Ovis aries Ovar-DRB1*1303 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATTCTACGAGCGAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTGCTGGA
CAGATACTTCCATAATGGAGAAGAGTCCGTGCGCTTCGACAGCGACTGGGGCGAGTTCCG
GGCGGTGGCCGAGCTGGGGCGGCCGGAGCGCTGAGTATTGGAACAGCCAGAAGGACTTCCT
GGAGAGCAGGAGGACCGCGGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB017226|AB017226.1 Ovis aries Ovar-DRB1*0132 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATACTAAGAAAGAGTGTTCGTTTCTTCAACGGGACGGAGCGGGTGCGGTACCTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGAGCGCCAAGTACTGGAACAGCCAGAAGGAGCTCCT
GGAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB017227|AB017227.1 Ovis aries Ovar-DRB1*0131 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATACTAAGAAAGAGTGTTCGTTTCTTCAACGGGACGGAGCGGGTGCGGTTTCCTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGAGCGCCAAGTACTGGAACAGCCAGAAGGAGCTCCT
GGAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACCTACGGGGTTCGGTGA

>ENA|AB017228|AB017228.1 Ovis aries Ovar-DRB1*0332 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATCATAAGAGCGAGTGTTCGTTTCTTCAACGGGACGGAGCGGGTGCGGTACCTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTTCCG
GGCGGTGGCCGAGCTGGGGCGGCCGGAGCGCCGAGTACTGGAACAGCCAGAAGGACTTCCT
GGAGCGGAAGCGGGCCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB017229|AB017229.1 Ovis aries Ovar-DRB1*0331 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATCATAAGAGCGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTACCTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTTCCG
GGCGGTGGCCGAGCTTGGGCGGCCGGACGCCGAGTACTGGAACAGCCAGAAGGACTTCCT
GGAGCGGAAGCGGGCCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB017230|AB017230.1 Ovis aries Ovar-DRB1*01072 gene for DR beta-chain antigen binding domain, partial cds.

GGAGTATACTAAGAAAGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTTCCTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGATCCT
GGAGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB061317|AB061317.1 Ovis aries Ovar-DRB1*0606 gene for MHC class II DR-beta-chain, partial cds.

GGAGTATCGTAAGAGCGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTACCTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGCTCCT
GGAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB061318|AB061318.1 Ovis aries Ovar-DRB1*0413 gene for MHC class II DR-beta-chain, partial cds.

GGAGTATCGTAAGAGCGAGTGTTCGTTTCTTCAACGGGACGGAGCGGGTGCGGTTCCTGGA
AAGATACTTCCATAATGGAGAAGAGACCCTGCGCTTCGACAGCGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAAGAGCTCCT
GGAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB061319|AB061319.1 Ovis aries Ovar-DRB1*0413 gene for MHC class II DR beta-chain, partial cds.

GGAGTATCGTAAGAGCGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTACCTGGA
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGACGCCGAGTACTGGAACAGCCAGAAGGAGCTCCT
GGAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACCTACGGGGTCTTTGA

>ENA|AB061320|AB061320.1 Ovis aries Ovar-DRB1*0414 gene for MHC class II DR beta-chain, partial cds.

GGAGTATCATAAGAGCGAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCCTGGA
CAGATACTTCCATAATGGAGAAGAGACCCTGCGCTTCGACAGCGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAAGAGCTCCT
GGAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB061321|AB061321.1 Ovis aries Ovar-DRB1*1302 gene for MHC class II DR beta-chain, partial cds.

GGAGTATTCTACGAGCGAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCCTGGA
CAGATACTTCCATAATGGAGAAGAGTTCGTGCGCTTCGACAGCGACTGGGGCGAGTTCCG
AGCGGTGGCCGAGCTGGGGCGGCCGGACGCCGAGTATTGGAACAGCCAGAAGGACTTCCT
GGAGAGCAGGAGGACCGCGGTGGACACGTACTGCAGACACAACCTACGGGGTCAATGA

>ENA|AB061322|AB061322.1 Ovis aries Ovar-DRB1*0351 gene for MHC class II DR beta-chain, partial cds.

GGAGTATCATAAGAGCGAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCCTGGA
CAGATACTTCCATAATGGAGAAGAGTTCGTGCGCTTCGACAGCGACTGGGGCGAGTTCCG
GGCGGTGGCCGAGCTGGGGCGGCCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGCTCCT
GGAGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB061323|AB061323.1 Ovis aries Ovar-DRB1*0141 gene for MHC class II DR beta-chain, partial cds.

GGAGTATACTAAGAAAGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTTCCTGGA
CAGATACTTCCATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGATCCT
GGAGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTTCATTGA

>ENA|AB061372|AB061372.1 Ovis aries Ovar-DRB1*03011 gene for MHC class II DR beta-chain, partial cds.

GGAGTATCATAAGAGCGAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGA
CAGATACTTCCATAATGGAGAAGAGTTCGTGCGCTTCGACAGCGACTGGGGCGAGTTCCG
GGCGGTGGCCGAGCTGGGGCGGCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGCTCCT
GGAGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCTTTGA

>ENA|AF036558|AF036558.1 Ovis aries Finnsheep MHC class II antigen Ovar-
DRB1 gene (Ovar-DRB1*0204 allele), partial cds.

GAGTATTCTACGAGCGAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGCGGAGCGCCGAGCACTGGAACAGCCAGAAGGAGCTCCTG
GAGCGGAGGCGGGCCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCTTGAGAGT
TTCAGTGTG

>ENA|AF036559|AF036559.1 Ovis aries Russian local sheep breed MHC class
II antigen Ovar-DRB1 gene (Ovar-DRB1*0322 allele), partial cds.

GAGTATCATAAGAGCGAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGG
GCGGTGGCCGAGCTGGGGCGGCGGAGCGCCGAGCACTGGAACAGCCAGAAGGAGCTCCTG
GAGAGCAGGAGGACCGCGGTGGACACGTACTGCAGACACAACCTACGGGGTCTTGAGAGT
TTCAGTGTG

>ENA|AF036560|AF036560.1 Ovis aries Finnsheep MHC class II antigen Ovar-
DRB1 gene (Ovar-DRB1*0205 allele), partial cds.

GAGTATTCTACGAGCGAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGCGGAGCGCCGAGCACTGGAACAGCCAGAAGGAGATCCTG
GAGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCTTTGAGAGT
TTCAGTGTG

>ENA|AF036561|AF036561.1 Ovis aries Romanov MHC class II antigen Ovar-
DRB1 gene (Ovar-DRB1*0115 allele), partial cds.

GAGTATACTAAGAAAGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGATCCTG
GAGCGGAAGCGGGCCCGCTGGACACGTACTGCAGACACAACCTACGGGGTCTTGAGAGT
TTCAGTGTG

>ENA|AF036562|AF036562.1 Ovis aries Finnsheep MHC class II antigen Ovar-
DRB1 gene (Ovar-DRB1*0116 allele), partial cds.

GAGTATACTAAGAAAGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGATCCTG
GAGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCTTGAGAGT
TTCAGTGTG

>ENA|AF036563|AF036563.1 Ovis aries Romanov MHC class II antigen Ovar-
DRB1 gene (Ovar-DRB1*0323 allele), partial cds.

GAGTATCATAAGAGCGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTACCTGGAC
AGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGTTCCTG
GAGCAGACGCGGGCCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCTTGAGAGT
TTCAGTGTG

>ENA|AF036564|AF036564.1 Ovis aries Finnsheep MHC class II antigen Ovar-
DRB1 gene (Ovar-DRB1*0323 allele), partial cds.

GAGTATCATAAGAGCGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGTTCCTG
GAGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCTTGAGAGT
TTCAGTGTG

>ENA|AF126432|AF126432.1 Ovis aries strain breed Latxa MHC class II DR
beta chain (DRB1) gene, partial cds.

AGTATAGTAAGAGCGAGTGTCATTTCTTCAACGGGACCGAGCGGGTGCGGTTTCCTGGACA
GATACTACACTAACGGAGAAGAGAACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCGGG
CGGTGACCGAGCTGGGGCGGCCGGACGCTGAGCAATGGAACAGCCAGAAGGACTTCCTGG
AGAGCAGGAGGACCGCGGTGGACACGTACTGCAGACACAACCTACGGGGTCTTT

>ENA|AF126433|AF126433.1 Ovis aries strain breed Latxa; sec-b MHC class
II DR beta chain (DRB1) gene, partial cds.
AGTATCATAAGAGCGAGTGTCATTTCTTCAACGGGACCGAGCGGGTGCGGTTTCCTGGACA
GATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCGGG
CGGTGGCCGAGCTGGGGCGGCAGAGCGCCGAGTACTGGAACAGCCAGAAGGAGCTCCTGG
AGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCTT

>ENA|AF126434|AF126434.1 Ovis aries strain breed Latxa; sec-c MHC class
II DR beta chain (DRB1) gene, partial cds.
AGTATACTAAGAAAGAGTGTCGTTTCTCCAACGGGACCGAGCGGGTGCGGTTTCCTGGACA
GATACTTCCATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGAG
CGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGCTCCTGG
AGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCAAT

>ENA|AF126435|AF126435.1 Ovis aries strain breed Latxa; sec-d MHC class
II DR beta chain (DRB1) gene, partial cds.
AGTATACTAAGAAAGAGTGTCGTTTCTCCAACGGGACCGAGCGGGTGCGGTTTCCTGGACA
GATACTTCCATAATGGAGAAGAGACCTGCGCTTCGACAGCGACTGGGGCGAGTACCGAG
CGGTGGCCGAGCTGGGGCGGCCGGACGCCGAGTACTGGAACAGCCAGAAGGACTTCCTGG
AGCGGGCGCGGGCCCGCTGGACACGTACTGCAGACACAACCTACGGGGTCTGGT

>ENA|AF126436|AF126436.1 Ovis aries strain breed Latxa; sec-g MHC class
II DR beta chain (DRB1) gene, partial cds.
AGTATCATAAGAGCGAGTGTCGTTTCTCCAACGGGACCGAGCGGGTGCGGTACCTGGACA
GATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCGAG
CGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGATCCTGG
AGCGGAAGCGGGCCCGCTGGACACGTACTGCAGACACAACCTACGGGGTCAAT

>ENA|AF126437|AF126437.1 Ovis aries strain breed Latxa; sec-a MHC class
II DR beta chain (DRB1) gene, partial cds.
AGTATCATAAGAGCGAGTGTCATTTCTTCAACGGGACCGAGCGGGTGCGGTTTCCTGGACA
GATACTTCCATAATGGAGAAGAGTTTCGTGCGCTTCGACAGCGACTGGGGCGAGTTCCGGG
CGGTGGCCGAGCTGGGGCGGCCGGAGCGCCGAGCACTGGAACAGCCAGAAGGAGCTCCTGG
AGCGGAGGCGGGCCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCAAT

>ENA|AF126438|AF126438.1 Ovis aries strain breed Latxa; sec-ap MHC class
II DR beta chain (DRB1) gene, partial cds.
AGTATCATAAGAGCGAGTGTCATTTCTTCAACGGGACCGAGCGGGTGCGGTTTCCTGGACA
GATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCGGG
CGGTGGCCGAGCTGGGGCGGCAGAGCGCCGAGCACTGGAACAGCCAGAAGGAGCTCCTGG
AGCGGAGGCGGGCCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCAAT

>ENA|AF126439|AF126439.1 Ovis aries strain breed Latxa; sec-j MHC class
II DR beta chain (DRB1) gene, partial cds.
AGTATCATAAGAGCGAGTGTCGTTTCTCCAACGGGACCGAGCGGGTGCGGTACCTGGACA
GATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCGAG
CGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGACTTCCTGG
AGCAGACGCGGGCCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCAAT

>ENA|AF126440|AF126440.1 Ovis aries strain breed Latxa; sec-h MHC class
II DR beta chain (DRB1) gene, partial cds.
AGTATACTAAGAAAGAGTGTCGTTTCTCCAACGGGACCGAGCGGGTGCGGTTTCCTGGACA
GATACTTCTATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGAG
CGGTGGCCGAGCTGGGGCGGCCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGATCCTGG
AGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCAAT

>ENA|AF126441|AF126441.1 Ovis aries strain breed Latxa; sec-f MHC class
II DR beta chain (DRB1) gene, partial cds.

AGTATAGTAAGAGCGAGTGTTCATTTCTTCAACGGGACCGAGCGGGTGCGGTTCTTGACAC
GATACTACACTAACGGAGAAGAGAACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCGGC
CGGTGACCGAGCTGGGGCGGCCGGACGCTGAGCAATGGAACAGCCAGAAGGACTTCCTGG
AGAGCAGGAGGACCGCGGTGGACACGTACTGCAGACACAACCTACGGGGTCTTT

>ENA|AF324840|AF324840.1 Ovis canadensis MHC class II beta chain (DRB)
gene, DRB*1 allele, exon 2 and partial cds.

GAGTATTATAAGGGCGAGTGTTCATTTCTTCAACGGGACCGAGCGGGTGCGGTTGCTGCAC
AGATTCTACACTAATGGAGAAGAGACCGTGCCTTCGACAGCGACTGGGGCGAGTTCCGG
GCGGTGACCCAGCAGGGACAGGAGGACGCCGAGCACTGGAACAGCCAGAAGGAGATCCTG
GAGCAGAAGCGGGCCGAGGTGGACACGGTGTGCAGACACAACCTATGGGGTCTTTGAGAGT
TTCCTGTG

>ENA|AF324841|AF324841.1 Ovis canadensis MHC class II beta chain (DRB)
gene, DRB*2 allele, exon 2 and partial cds.

GAGTATTATAAGGGCGAGTGTTCATTTCTTCAACGGGACCGAGCGGGTGCGGTTGCTGCAC
AGATTCTACACTAATGGAGAAGAGACCGTGCCTTCGACAGCGACTGGGGCGAGTTCCGG
GCGGTGACCCAGCAGGGGACAGGAGGACGCCGAGCACTGGAACAGCCAGAAGGAGATCCTG
GAGCAGAAGCGGGCCGAGGTGGACACGGTGTGCAGACACAACCTATGGGGTCTTTGAGAGT
TTCCTGTG

>ENA|AF324842|AF324842.1 Ovis canadensis MHC class II beta chain (DRB)
gene, DRB*3 allele, exon 2 and partial cds.

GAGTATTATAAGGGCGAGTGTTCATTTCTTCAACGGGACCGAGCGGGTGCGGTTGCTGCAC
AGATTCTACACTAATGGAGAAGAGACCGTGCCTTCGACAGCGACTGGGGCGAGTTCCGG
GCGGTGACCCAACAGGGGACAGGAGGACGCCGAGCACTGGAACAGCCAGAAGGAGATCCTG
GAGCAGAAGCGGGCCGAGGTGGACACGGTGTGCAGACACAACCTATGGGGTCTTTGAGAGT
TTCCTGTG

>ENA|AF324843|AF324843.1 Ovis canadensis MHC class II beta chain (DRB)
gene, DRB*4 allele, exon 2 and partial cds.

GAGTATTATAAGGGCGAGTGTTCATTTCTTCAACGGGACCGAGCGGGTGCGGTTGCTGCAC
AGATTCTACACTAATGGAGAAGAGACCGTGCCTTCGACAGCGACTGGGGCGAGTTCCGG
GCGGTGACCCAGCAGGGGACAGGAGGACGCCGAGCACTGGAACAGCCAGAAGGAGATCCTG
GAGCAGAAGCGGGCCGAGGTGGACACGGTGTGCAGACACAACCTATGGGGTCTTTGAGAGT
TTCATTGTG

>ENA|AF324844|AF324844.1 Ovis canadensis MHC class II beta chain (DRB)
gene, DRB*5 allele, exon 2 and partial cds.

GAGTATACTAAGAAAGAGTGTCTGTTTCTCCAACGGGACCGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGAACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGG
GCGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGTCTCTG
GAGCGGAGGCGGGCCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCTTTGAGAGT
TTCCTGTG

>ENA|AF324845|AF324845.1 Ovis canadensis MHC class II beta chain (DRB)
gene, DRB*6 allele, exon 2 and partial cds.

GAGTATACTAAGAAAGAGTGTCTGTTTCTCCAACGGGACCGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGG
GCGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGTCTCTG
GAGCGGAGGCGGGCCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCTTTGAGAGT
TTCCTGTG

>ENA|AF324846|AF324846.1 Ovis canadensis MHC class II beta chain (DRB)
gene, DRB*7 allele, exon 2 and partial cds.

GAGTATACTAAGAAAGAGTGTCTGTTTCTCCAACGGGACCGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGG
GCGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGTCTCTG
GAGCGGAGGCGGGCCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCTTTGAGAGT
TTCCTGTG

>ENA|AF324847|AF324847.1 Ovis canadensis MHC class II beta chain (DRB)
gene, DRB*8 allele, exon 2 and partial cds.

GAGTATACTAAGAAAGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGAACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGG
GCGGCGGGCCGAGCTGGGGCGGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGCTCCTG
GAGCGGAGGCGGGCCGAGGTGGACACGTACTGCAGACACAACACTACGGGGTTCGGTGAGAGT
TTCAGTGTG

>ENA|AF324848|AF324848.1 Ovis canadensis MHC class II beta chain (DRB)
gene, DRB*9 allele, exon 2 and partial cds.

GAGTATCATAAGAGCGAGTGTTCGTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGCTCCTG
GAGCGGAGGCGGGCCAATGTGGACACGTACTGCAGACACAACACTACGGGGTTCGGTGAGAGT
TTCAGTGTG

>ENA|AF324849|AF324849.1 Ovis canadensis MHC class II beta chain (DRB)
gene, DRB*10 allele, exon 2 and partial cds.

GAGTATCATAAGAGCGAGTGTTCATTTCTCCAACGGGACCGAGCGGGTGCGGTTGCTGGAC
AGATACTTCCATAATGGAGAAGAGTTTCGTGCGCTTCGACAGCGACTGGGGCGAGTTCCGG
GCGGTGGCCGAGCTGGGGCGGGCCGGCCGCGAGTACTACAACAGCCAGAAGGACTTCCTG
GAGAGCAGGAGGGCCGCGGTGGACACGTACTGCAGACGCAACTACGGGGTTCATTGAGAGT
TTCAGTGTG

>ENA|AF324850|AF324850.1 Ovis canadensis MHC class II beta chain (DRB)
gene, DRB*11 allele, exon 2 and partial cds.

GAGTATCATAAGAGCGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGG
GCGGTGGCCGAGCTGGGGCGGGCCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGCTCCTG
GAGCGGAGGCGGGCCGAGGTGGACACGTACTGCAGACACAACACTACGGGGTTCATTGAGAGT
TTCAGTGTG

>ENA|AF324851|AF324851.1 Ovis canadensis MHC class II beta chain (DRB)
gene, DRB*12 allele, exon 2 and partial cds.

GAGTATCATAAGAGCGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTACCTGGAC
AGATACTTCCATAATGGAGAAGAGTTTCGTGCGCTTCGACAGCGACTGGGGCGAGTACCGG
GCGGTGGCCGAGCTGGGGCGGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGATCCTG
GAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACACTACGGGGTCTTTGAGAGT
TTCAGTGTG

>ENA|AF324852|AF324852.1 Ovis canadensis MHC class II beta chain (DRB)
gene, DRB*13 allele, exon 2 and partial cds.

GAGTATCATAAGAGCGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTACCTGGAC
AGATACTTCCATAATGGAGAAGAGTTTCGTGCGCTTCGACAGCGACTGGGGCGAGTACCGG
GCGGTGGCCGAGCTGGGGCGGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGATCCTG
GAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACACTACGGGGTCTTTGAGAGT
TTCAGTGTG

>ENA|AF324853|AF324853.1 Ovis canadensis MHC class II beta chain (DRB)
gene, DRB*14 allele, exon 2 and partial cds.

GAGTATCATAAGAGCGAGTGTTCATTTCTCCAACGGGACCGAGCGGGTGCGGTTGCTGGAC
AGATACTTCCATAATGGAGAAGAGTTTCGTGCGCTTCGACAGCGACTGGGGCGAGTTCGG
GCGGTGGCCGAGCTGGGGCGGGCCGGCCGCGAGTACTACAACAGCCAGAAGGACTTCCTG
GAGAGCACGAGGGCCGCGGTGGACACGTACTGCAGACACAACACTACGGGGTTCATTGAGAGT
TTCAGTGTG

>ENA|AF324854|AF324854.1 Ovis canadensis MHC class II beta chain (DRB)
gene, DRB*15 allele, exon 2 and partial cds.

GAGTATCATAAGAGCGAGTGTTCGTTTCTTCAACGGGACGGAGCGGGTGCGGTACCTGGAC
AGATACTTCTATAATGGAGAAGAGAACGTGCGCTTCGACAACGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGCTCCTG
GAGCGGAGGCGGGCCGAGGTGGACACGTACTGCAGACACAACACTACGGGGTCTTTGAGAGT
TTCAGTGTG

>ENA|AF324855|AF324855.1 *Ovis canadensis* MHC class II beta chain (DRB) gene, DRB*16 allele, exon 2 and partial cds.
GAGTATCGTAAGAGCGAGTGTCTGTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGGCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGCTCCTG
GAGCGGAGGCGGGCCGAGGTGGACACGTACTGCAGACACAACACTACGGGGTTCGGTGAGAGT
TTCAGTGTG

>ENA|AF324856|AF324856.1 *Ovis canadensis* MHC class II beta chain (DRB) gene, DRB*17 allele, exon 2 and partial cds.
GAGTATGCTAAGAGCGAGTGTCTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGAACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGGCGGACGCCAAGTACTGGAACAGCCAGAAGGAGCTCCTG
GAGCAGACGCGGGCCGAGGTGGACACGTACTGCAGACACAACACTACGGGGTCTTTGAGAGT
TTCAGTGTG

>ENA|AF324857|AF324857.1 *Ovis canadensis* MHC class II beta chain (DRB) gene, DRB*18 allele, exon 2 and partial cds.
GAGTATGCTAAGAGCGAGTGTCTGTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGAA
AGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGGCGGACGCCAAGTACTGGAACAGCCAGAAGGAGATCCTG
GAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACACTACGGGGTTCGGTGAGAGT
TTCAGTGTG

>ENA|AF324858|AF324858.1 *Ovis canadensis* MHC class II beta chain (DRB) gene, DRB*19 allele, exon 2 and partial cds.
GAGTATGCTAAGAGCGAGTGTCTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGAACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGGCGGACGCCAAGTACTGGAACAGCCAGAAGGACTTCCTG
GAGCGGAAGCGGGCCCGCTGGACACGTACTGCAGACACAACACTACGGGGTCTTTGAGAGT
TTCAGTGTG

>ENA|AF324859|AF324859.1 *Ovis canadensis* MHC class II beta chain (DRB) gene, DRB*20 allele, exon 2 and partial cds.
GAGTATGCTAAGAGCGAGTGTCTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGAACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGGCGGACGCCAAGTACTGGAACAGCCAGAAGGAGCTCCTG
GAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACACTACGGGGTCTTTGAGAGT
TTCAGTGTG

>ENA|AF324860|AF324860.1 *Ovis canadensis* MHC class II beta chain (DRB) gene, DRB*21 allele, exon 2 and partial cds.
GAGTATGCTAAGAGCGAGTGTCTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGAACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGGCGGACGCCAAGTACTGGAACAGCCAGAAGGAGCTCCTG
GAGCAGACGCGGGCCGAGGTGGACAGGTACTGCAGACACAACACTACGGGGTCTTTGAGAGT
TTCAGTGTG

>ENA|AF324861|AF324861.1 *Ovis canadensis* MHC class II beta chain (DRB) gene, DRB*22 allele, exon 2 and partial cds.
GAGTATCATAAGAGCGAGTGTCTGTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCTATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGG
GCGGTGGCCGAGCTGGGGCGGGCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGCTCCTG
GAGCGGGCGGGCCCGCTGGACACGTACTGCAGACACAACACTACGGGGTCTTTGAGAGT
TTCAGTGTG

>ENA|AJ968652|AJ968652.1 *Ovis canadensis* partial HLA-DRB gene for MHC class II antigen, HLA-DRB*1 allele, exon 2
GAGTATGCTAAGAGCGAGTGTCTGTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGAA
AGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGGCGGACGCCAAGTACTGGAACAGCCAGAAGGAGATCCTG
GAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACACTACGGGGTTCGGTGAGAGT
TTCAGTGTG

>ENA|AJ968653|AJ968653.1 Ovis canadensis partial HLA-DRB gene for MHC class II antigen, HLA-DRB*2 allele, exon 2
GAGTATTATAAGGGCGAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCGGTTGCTGCAC
AGATTCTACACTAATGGAGAAGAGACCGTGCCTTCGACAGCGACTGGGGCGAGTTCCGG
GCGGTGACCCAACAGGGGACAGGAGGACGCCGAGCACTGGAACAGCCAGAAGGAGATCCTG
GAGCAGAAGCGGGCCGAGGTGGACACGGTGTGCAGACACAACCTATGGGGTCGTTGAGAGT
TTCACTGTG

>ENA|AM180935|AM180935.1 Ovis aries mRNA for MHC DR beta chain (ovar-MHCII-DRB1 gene), ovar-MHCII-DRB1*0101 allele
TTCTCCAGCATGGTGTGCCTGTATTTCTCCAGAGGCTCCCGGATGGCAGCTCTGATAGTG
ATGCTGATGGCGCTGAGCCCTCCCTGGCCTGGGCCAGGAAGATCCAACCACATTTCTTG
GAGTATACTAAGAAAGAGTGTCTGTTTCTCCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCCATAATGGAGAAGAGACCTGCGCTTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGC
TGGGGCGGGCCGACGCCAAGTACTGGAACAGCCAGAAGGACTTCCTG
GAGCGGGCGCGGGCCCGCTGGACACGTACTGCAGACACAACCTACGGGGTCATTGAGAGT
TTCACTGTGCAGCGGCGAGTGGAGCCTATAGTGACTGTGTATCCTGCAAAGACCCAGCCC
CTGCAGCACCACAACCTCCTGGTCTGCTCTGTGAATGGATTCTACCCAGGCCACATTGAA
GTCAGGTAGGTTCCGGAATGGCCACGAAGAGGAGGCTGGGGTGATCTCCACAGGCCCTGATC
CAGAATGGAGACTGGACCTTCCAGACCATGGTGATGCTTGAAACAGTTTCCTCAGAGTGGA
GAGGTCTACACCTGCCAAGTGGATCACCCAGCCGGACGAGCCCTATCACAGTGGAAATGG
AGGGCACGGTCTGACTCAGCTCAGAGCAAGATGATGAGTGGAGTTGGGGGCTTTGTTCTG
GGTCTGCTCTTCCTTGCGGTGGGGCTCTTCATCTACTTCAGGAATCAGAAAGGACGCCCT
ACCCTTCAGCCAACAGGGCTCCTGAGCTGAAGTGACGAT

>ENA|AM180936|AM180936.1 Ovis aries mRNA for MHC class II antigen, Ovar-DRB1*0501 allele
TTCTCCAGCATGGTGTGCCTGTATTTCTCCAGAGGCTCCCGGATGGCAGCTCTGATAGTG
ATGCTGATGGCGCTGAGCCCTCCCTGGCCTGGGCCAGGAAGATCCAACCACATTTCTTG
GAGTATGCTAAGAGCGAGTGTCTGTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGAA
AGATACTTCTATAATGGAGAAGAGACCTGCGCTTCGACAGCGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGGCCGACGCCAAGTACTGGAACAGCCAGAAGGAGCTCCTG
GAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGAGAGT
TTCACTGTGCAGCGGCGAGTGGAGCCTATAGTGACTGTGTATCCTGCAAAGACCCAGCCC
CTGCAGCACCACAACCTCCTGGTCTGCTCTGTGAATGGATTCTACCCAGGCCACATTGAA
GTCAGGTAGGTTCCGGAACGGCCACGAAGAGGAGGCTGGGGTGATCTCCACAGGCCCTGATC
CAGAATGGAGACTGGACCTTCCAGACCATGGTGATGCTTGAAACAGTTTCCTCAGAGTGGA
GAGGTCTACACCTGCCAAGTGGATCACCCAGCCGGACGAGCCCTATCACAGTGGAAATGG
AGGGCACGGTCTGACTCAGCTCAGAGCAAGATGATGAGTGGAGTTGGGGGCTTTGTTCTG
GGTCTGCTCTTCCTTGCGGTGGGGCTCTTCATCTACTTCAGGAATCAGAAAGGACGCCCT
ACCCTTCAGCCAACAGGGCTCCTGAGCTGAAGTGACGAT

>ENA|AM180937|AM180937.1 Ovis aries mRNA for MHC class II antigen, Ovar-DRB1*0301 allele
TTCTCCAGCATGGTGTGCCTGTATTTCTCCAGAGGCTCCCGGATGGCAGCTCTGATAGTG
ATGCTGATGGCGCTGAGCCCTCCCTGGCCTGGGCCAGGAAGATCCAACCACATTTCTTG
GAGTATACTAAGAAAGAGTGTCTGTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGAC
AGATACTTCCATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGA
GCGGTGGCCGAGCTGGGGCGGGCCGACGCCAAGTACTGGAACAGCCAGAAGGAGATCCTG
GAGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCATTGAGAGT
TTCACTGTGCAGCGGCGAGTGGAGCCTATAGTGACTGTGTATCCTGCAAAGACCCAGCCC
CTGCAGCACCACAACCTCCTGGTCTGCTCTGTGAATGGATTCTACCCAGGCCACATTGAA
GTCAGGTAGGTTCCGGAATGGCCACGAAGAGGAGGCTGGGGTGATCTCCACAGGCCCTGATC
CAGAATGGAGACTGGACCTTCCAGACCATGGTGATGCTTGAAACAGTTTCCTCAGAGTGGA
GAGGTCTACACCTGCCAAGTGGATCACCCAGCCGGACGAGCCCTATCACAGTGGAAATGG
AGGGCACGGTCTGACTCAGCTCAGAGCAAGATGATGAGTGGAGTTGGGGGCTTTGTTCTG
GGTCTGCTCTTCCTTGCGGTGGGGCTCTTCATCTACTTCAGGAATCAGAAAGGACGCCCT
ACCCTTCAGCCAACAGGGCTCCTGAGCTGAAGTGACGAT

>ENA|AM180938|AM180938.2 Ovis aries mRNA for MHC class II antigen, Ovar-DRB1*0901 allele

TTCTCCGGCATGGTGTGCCTGTATTTCTCCAGAGGCTCCCGGATGGCAGCTCTGATAGTG
 ATGCTGATGGTGCTGAGCCCTCCCCTGGCCTGGGCCAGGGAGATCCAACCACATTTTCCTG
 GAGTATTATAGGAGCGAGTGTCAATTTCTTCAACGGGACCGAGAGGGTGC GGCTCCTTGAA
 AGATACTTCCATAATGGAGAAGAGTTTCGCGCGCTTCGACAGTACTGGGGCGAGTTTCGG
 GCAGTGACCGAGCTGGGGAGGCCGGCCGCTGAGCAATGGAACAGCCAGAAGAACATCCTG
 GAGCAGAAGCGGGCCGAGGTGAACACGGTGTGCAGACACAACCTATGGGGTCTTTGAGAGT
 TTGCTGTGCAGCGGCGAGTGGAGCCTATAGTGACTGTGTATCCTGCGAAGACCCAGCCC
 CTGCAGCACCACAACCTCCTGGTCTGCTCTGTGAACGGATTCTACCCAGGCCACATTGAA
 GTCAGGTGGTTCCGAAACGGCCATGAAGAGGAGGCTGGGGTGATCTCCACAGGCCCTGATC
 CAGAATGGAGACTGGACCTTCCAGACCATGGTGATGCTTGAAACAGTTCCTCAGAGTGGA
 GAGGTCTATACCTGCCAAGTGGAGCACCCAGCCGGATGAGCCCTATCAGAGTAGAATGG
 AGGGCACGGTCTGACTCTGCTCAGAGCAAGATGATGAGTGGAGTTGGGGGCTTTGTGCTG
 GGTCTGCTCTTCCTTGCAGTGGGACTCTTCATCTACTTCAGGAATCAGAAAGGACGCCCT
 ACACCTCAGCCAACAGGGCTCCTGAGCTGAAGTGAAGAT

>ENA|AM884914|AM884914.1 *Ovis aries* Ovar-DRB1 gene for MHC class II
 antigen, Ovar-DRB1*0401 allele, exons 1-6

CTTTGACCAGCACAAAGCTAGATCACAATAGGGGCCAGTTAAAAATATTTTCAGATGCAAC
 AGGGTCAAATCTTTAAGTACTAAATTAACAATCCTTTTAGTGAGAAAAATTTCTACG
 TTTTCAGAAAGACCTTCATATTGAATCTCTGACCAGCAACTGATGCTATTTGCCTC
 TGATGTTGATTGGTTGCCTAGACTGGGCTCACCAATCCAGGAGCAAAATGAGTTCCTTGG
 TTGGTATTACTTGAGATGTGGGTGAAGGGGGTCACAGTACCCATTTGAGAGGGACTTGCC
 TGCTCCTCTCCCTCTCTATCCTCTGCTGTTCTCCAGCATGGTGTGCCTGTATTTCTCCAG
 AGGCTCCCGGATGGCAGCTCTGATAGTGATGCTGATGGCGCTGAGCCCTCCCTTGGCCTG
 GGCCAGGAAGATCCAACGTAAGTTTATACCTTGGATGGTGACCTACCATGGGGTAGGGGG
 GTGGGGAGGAACAGAGTTAACTTTGTCACTACATCCAGGCCAGACCCCTTACAAACTGTG
 ATATATTCTTATTGACCACCTATCTTTATCATATGGATCCTTAGTTCCTTCCACAGTAAA
 GGAGCCTGAGTGCTTGCCCACTTAATGAGAGTTGTGTAAGTTGCCGCCGAATACATGAAC
 CATTTCTTTTCCAACCTCTCCTCCAATAAAACCTATCCAGCCTTGCAATTCATTTCTTAGG
 GTCTTAAGATTTATAAATAAGAATGTAAAAATAATTCCTCATACAGCAGTTTCCTTTATT
 TATAGTGTGTTGTGTGTGTTAGTCACTCAGTCATGTCTGACTCTTTGTGACCCCATGGAC
 TGTGGCCACCGGGCTCTTCTTTCCATGGGATTCTCCAGGCAAGAATACTGGAGTGGGCA
 GCCATTGTGCTCTCCAGGGGATCTCACAACCCGGGGATTGAACCTGGGTGTCCACATTG
 CAGGGCAGACTCTTTATAGTTTTAGCCACCAGTTATGCCAAAAAGGGCTTCCAGTGGT
 GCTAGGGGTGAAGAATCTGCCTGCCAATGCAAGAGATGTAAGAGATGGGGTTTGATCCCT
 GGATCAGGAAGATCTTCTGGAGAAGGAATGGCAACCCACTCCAGTATTCTTGCTTGAGAG
 ATCCCATTGGAAGAGCCTGGTGGGCTACAGTCCATGGGGTCGCAAGGGACAGACAC
 GACTGAAGCAATTTAGCATGCATGCCAAAAACGGGAAGTTTTCGCAAAAAGATTTCTGT
 GGATTCAAAAGAAATTAGAAAGATCTCTTCTAGAAGATCCTGTTGTGTCTCAATAGGAC
 CTATGCTGTCTCTCCTTAGTATGTAAGAATATATCAAAAAGGTCTCTCCCCATTAAGCTGT
 TTCCTTTCTCCTGAGCTCCAGTGTTTATAAGGATTATGTCCCTGTAATGGAAGTCTCTG
 ACAAAGTTGGGGTTGGTTTTCTCTCTATTCTGTGGAAGGACGCTAAAGCTTAAGCAGA
 GATTCTTAGTACTTGAATGACTCTATAGATAAGGAGCACCTTATGGGATGTTCTATGAC
 ACTTAAAGAATTACATAAATTCTGAAAACCTGACATAGGTTAGTATTCATCACAAGTCT
 ATTTTGAATCTTTCTGCACAATCAGTTTCTCCTACATCTCCCCATTCTCTGCCCTGAACC
 CATGAGAAGGGATTTAACTAGCGGAGGACAAATTATATAGAATTCTGTTTTGTAGTCA
 ATAGCAATCAATTATCAGCAATTTTCATGTTGTTCAAACCATAAAACCTAAGCAGGGTACA
 GAGTATGAAGGTTGTTTTCCATTGCATAGGGTTGAAAAGTCAAAAAGCAAGTCAAGGGGGTT
 CATTGGCCTGTTGAGGTCTTGGCCTCAAATTTTCATAGCTTCATTTATCATGTAGTCTCTG
 TTCCTTAATTATTTCATGTTAATAAATCTTTCCAGTTATTCCCTACTCCTTTTCCAGTTAT
 GTCATCACCATTATTGAAAATCCCCAAGTTTACACAGACCATCAGCACTATATAGTGCAT
 TAGATGAGATGAAATTTAGTGAAAATTTCTCTCTTTCTTAAAAATCACCTTTTACTTAAC
 TTTGAATGTTTCTTACAACCTAGTGGGAGGAGAAAGAGGAAATTTGTCTGAATTTGCCATA
 GAAGGTAGAAAGAAATTTAATGTGTCTATCAGAATAAAAGTGTTGGAGCTGGAGCCCCCTCT
 GGATGCTTTTCCAAGATCCCCACAAAAATCAGCTTCCAAAACCTCAGGGTTTATTTGTTTAG
 ACCAAAAATCTGTTTTTTTTTTTTTCTGAAATAGCAATTATATATTGGGCTCTGTTCTAG
 GCCCAGAACATTCTATTTGAATAAGGAAAAAAGACCCCTGCTATCATGGAGACAGGAGA
 GAAAGACAACAACCAATGAACCTTTAACAAGAAAAACATTTTCAGAGACAAATAAGTGCT
 CTGAAAAAATATGTCAGGGTCATGGAACAATGAGAATTGCATTCACCCGATTTTCAGTT
 CAGGTGGCTGGTAAAAATGACATTTAGTTGAAATATGAATGATGGAAAGCCAGTCATTGA
 AGGATGTAAGGGAACAGGATGAAGTGAGGAAGATACTTGATTTTCTAAAGGGACAAAAAA
 GAAGGCAAGAAAGTGGCTGAAGCATAGAAAGCAAGTTGGCATGTGGAATAAGATGAGGTT

GAAGATGAAGTCAGGGGACAAATCATATTAGGTCCTGATGGCTGTGGTAAAAACATTTAAA
TTAAAAAAAAAAGATATGTCAATGCTACTGAGGGATTGTTTCCAGGTGGCGCTACTGTT
AAAGAATCTGCATGCAAATGCAGGAGATGTAAGAGATGTAAGAGACATGGGTTTGATCCC
TACATCAGGAAGGTCCCCTGGAGGAGGAAATGGTAACGACTCCAGTATTTCTTGCCCGGG
AACTCCATGAACAGAGAGCCTGGGGGGCTACAGTCCATGGGGTCGCAAGAGTCCAGACA
TGATTTGAGCACAGCACAGCACTGAGGGATTAGGAAGAAAGTCACTTGGTGGTGTGTTTT
ATTGAAATAGGAAAAGTTTTTGAAGGAAATAATTTGAAGTGGGTAGATAGAAGATAAGT
TTTGTGTTATTTTAAAGTTTGAAATAATTTATTAACGTGTATGTGGAGCCTTCAAGAAGTCA
ATTGAAAACATCAAATTGGAATTCAGAGGAGGCCAGAGCCAAAGGTATGTGTGTCAGGG
TCATTGACATATGCACTGTGTTAAAATATAAGAAAGTAGGGGAAGGAGACGGAGAAGGCA
ATGGCACGCCACTCCAGTACTCTTGCTGGAAAATCCCATGGATGGAGGAGCCTGGTAGG
CTGCAGTCCATGGGGTCGTGAAGAGTCAGACATGACTGAGTGACTTCACTTTCACTTTTC
ACTTTCTTGCATTGGAGAAGGAAATGGCAACCCACTCCAGTGTCTTGCTGGAGAATCC
CAGGGATGTGGGAGCCTGGTGGGCTGCCGTCTATGGGGTCGCACAGAGTAGGACACGACT
GAAGCGACTTAGCAGCAGCAGCAGCAGGGGAAAGGAGAGAGTGTGTGTAGATCAGAAAAAG
AGAGCAAGGGCCATGTCCAGAGGGCCAAGGGCTTATGAGTCTGTAAAAAGAGCCTGCGAAG
GGGTACTGTTGATATTGGGGAAAACCAAGAGAATGTGATGCATGCAAGTGAAGAAAAATTT
TTCAAGAAGGGAAGGAGTGGCAGTTGTGGTGAGTTTGACTAAGGAGGGTCAAGTGAGAAC
ATGACAAAAGAAATCAGCACTGGGTTTGGAGGACTTGATGTTTACAGTCAATAGAACATAC
AAGACAGGAGCTAGATTGGACCCTCTGAAGAAAGAATGAGAGCTGAAGAAAGTGAGGAATG
GATTACAGGATGCCACATTTGAGTAGCTTAAATCAGGGGGAAGTGTGCCGTAGAATCAGA
GAGTAAGCTGGACCTAAAGTATAAGAATAAAAGAACCTGAAGAAATGCTAGGAAGACTTG
AGAACCAGAGAGGTTTCAAGTACCAGCAAAAAACACTAGAATGCCCTTGATGTATGCAAG
GGTGAAGTGGTTATGGAAAAAGCCATTGATTTATACAACTTATATTTATTAGTGACCTAA
TGTACAACAGTTATTCCCCTAGCTGATGAGATTGGAGTAACAAAACAAAAACCCCAATCT
CTATCAGCATGGAACATCAAAGCACTTCATAGTTGTTACGTACCAGCCTTGTTACGTACC
AGGTCCATAAATTTTCAAGCATGTAATTTCTTATAACTGTCTATCGAATCTGTAGCAATTAA
AATATATCTGTGGAATCTAATATTCAAAAAGTTTCAATAATTTACCCAGTGTACATAGT
TGCTGCTAGAGCCAGATTATATAGCGTGAAACTGAGTTTATGGAAATTCCTTTTCTTTT
ATGTCAGCATACTCTGTTTGTGTTAGAGTCATATATACATTATTTTATAGAAAGCAA
TGTTTTCTGCTCTTTTATACAAAATGGTAATTAGTGATAAAATTAATTGAAGACAGTTGCC
AGATGATGATGAAGATATCACTTGCTTTAGCAAGTAAACAAGTAGATCTTGTGAGCTCAC
ATTCATAGGGTTTATAAAAAATTAATGGCAATGTATTTATTGAGTACTTATGATATGAA
CAGCACTAGAAAGACTGCTAGAAAGCAATAAATAGGAGGAATATTCATTAATTTTGCATTT
ATTTTACAAGTTTCATATGGGTAAATAGTGTATGTGCAGGCTGTGCATGGGCATGTGAAGA
AGAAGAAAAAGAAGTATTAAAGGTATTCCTTCTGAAATTTTGTAGCAAGTTGGGCTAAG
GTTGCCAAATATAACACAGGATCCAGTTAAATTTAAATTTTAGCTAAACAACAATAGTTT
CTGAAATACAAATTTAACTGGGAAATCTGTCTTTTATTTACTAAATTTGGCAACCTTAAA
TTGGGCACATGAGTTGCAGTAACAGTGCTAACCCACATAAGCTACCATAAAAAATTGACCT
CGCACAGTTTTATTTTTTAACTTTGTCTTTGACCAAGAGGTATTAGAGAATTTGTGATAT
TAAGATAGACTTGGTCTGATTCACAGTGCACCTTTCTGCCATCATTTATAAGTGAAAGTCT
CTTCTCAGAGTCTGGGGAATTGCTCATTTCTTGTTAACTGTCTAAATGAGGTCACTTTCT
CCCTTTCTTTCTTTCTTTCCAATGGGACTTGACTACAGAAATAAGAATTCCTTTGTATGAC
CAAGGCTGATAATTTAATGCCTACTGGTATTATTGGGAGTAGGAGACAAAGTTAGAAAAT
GAATTATTTGGGGCTTTGAATGGGAATAAAATGTCTGTGACTGTAGTTTACTCCTATACT
ATAGACAAGTAGTGGGTCAAGTGGCAGAGAAATCAAGAAGGAAGATGATGTGAAGGATAAA
TTACATGACTTTGTAATTTGTTGGTGAGGGAAACAAAGAAGGCTTTGTACTGAATAAATG
TGTTTTTACTAGGAAAGTAGCTCTCCACTGGGGCTGGATTCTTAAAAAGTATAGATTTGAT
ATAGGACCAAGACAGACTATTGGCAAACTTTCAATGTAATTTCTCAGCTGCTCCAAAATT
AACAATGGTTTTTTGCACCGTAGATTTTTTTTTCAGATGGGTTTATACTGATGGAGCTCATCTG
GTGATGAACCACCACTCCTTACTCCTACTCCTTGACTCCTAAACATTTGGAAAATATCTGG
AGCCATTTTTTGGTTGTTACACTGAGGGTTTCTTCTGACATCCACTATGTAGGGGTAAGGG
ATGCTGGTAAACAGCCTACCATGTACCGAACAGACACCATCCCAACCCCTCAGAGCCATAT
TTGACCCCTTAACTCATCAAGTCAGATTTGCCAATTGAGATTGTCACCAATTTTTTAAAAA
TCTGTTTTTCTGAGCTTTTATTAATTTGAAAATGCAGGAAAGAGATTGTAGCGCCATATTA
GGGTTTTTGGTTTTAATATCTTTTAAAGCTCCTCAGTAGTTTCCCTTACATATAGTATAAAG
TAAAAATCTTAACATCACCTACAGGACTTTTAAAGTTATTGGCTCAAGTACTTGATTTCTC
CAGTATAGTCTTTTACCTCCTCCCTCTCACTCTCTGCACTTCAATGAAATATTTTTTCTA
GTTCTTTTAAAGAAGTCCGTCACTTCTTCCAAGCTTTTGTACATGGTGTTAATGTACAAAA
TACAGACACCTGAAACACGTCTCCCTTTTACCCTAAACATACACACACACACCCAGTTTC
TTCCCTCAGTGCATGCCAATTAACATTTTATGTTACATTAAATGTTACTCTTAAGAGAC
CACTTTTTTGGCACCTAATGTAATTCAGGTCTATCCTATAATCGTTACAGAAGTCTAACACT
TCTGATATTTCTCATTCTTGTATAAATCTTTTATGGTTAATTTTGTCTATCATTTTTCA

212

TGCTGCTAAGTCGCGTTAGTCGTGTTCTGACTCTGTGCGACCCCATAGACGGAAGCCCCC
 AGGCTCCTCTGTCTCTGGGATTCTCCAGGCAAGAACACTGGAGTGGGTGCCATTTTCCTT
 CTCCAATGCATGAAAGTGAACAGTGAAGTGAAGTCCCTCAGTTGTGTCTGACTCTTAGC
 GGCCCCATGGAGCTGTAGCCTACCAGGCTTCTCCATCCATGCGATTTCCCAGGCAAGAGTA
 CTGGAGTGGGGTGCCATTGCCTTCTCCGCTAGACAAGCTACTTAACCTCATTGAGTCCTT
 GGCTCCTCGTCCATTAGATGTTGAAGACATGTGACCTAATAGCATGGGTGTGATATTTAA
 ATAAGTTCACCGTCTGAATCTTGTAGCTACTCAATGTGATTTTTTAATGTCTTTTCCAGAA
 ATGTCCAATTATTCTAATTCTTCCAGGGTAGCCTTCTTTCTCATTCTCATAGTTCACAA
 TTTTCAGAGTCTCAATTAGAGAAGACAATTTGGGATAAAAAATGACTAAAACTGGCTTCTTT
 TCTCAGGGGACCGGTCTGACTCAGCTCAGAGCAAGATGATGAGTGGAGTTGGGGGCTTTG
 TTCTGGGTCTGCTCTTCTTGCCTTGGGGTGGGGCTCTTCATCTACTTCAGGAATCAGAAAGGTA
 AGGAGCCTTTGGGCAGCTGAGCCTCCCCACTGACTTTTGGAGGAAGACATGTGGTTTTGC
 TCAAGTTAGTTCTCTGTATATCAATGGCCTTGTCTAAAGCTTGTTCCTTAACCTGACTTT
 AATATCCTGGAGATTCAGAAATGTGTAGTCCATGGTTACTTATGGGTGAAACATAAGAGA
 TTGTGGCTTGTAGAGATAAGGAAAGGTTAACATACATGGGGATTTGGGATGGAGATCCTG
 GGACAAATGCAGGAAGAGACAATAAAGCTGACTTAATTGCATTGGATTGGTATGAGACAA
 ACTTCATTGGTCACATGCTATCAGTGTTCACCTTCATATAAACCTGAAATCAGATGATA
 TGGGTATGGTATTAGGAAGATCTCGGGTGGGGCCCCGGGGCTTGGGACATTGTGTTTTG
 GGGATGGATCAACCTCTATATCTTTAAGTGTATATCTTCTTTGTCTCTCCTAGGACGC
 CCTACCCTTTCAGCCAACAGGTATGCTCTTTATCTTTTAGAATCGTGTTAGTCTCCCTGG
 AACATGATAGAGATAACAAGACAGAGGCAGAAATAATAAAAGACTTTGGACCTGACTT
 CTCATCAGGCAGTTTACACTAAAGTTTCTTCTTTCACTAAATAAAAGGCTTGTGCTCTA
 AAGTAGCTTTGGCTCAGGAAACTGAAGAATATTTTCCCTTCCAACCTGTAATGCTTTAAT
 ATTAACATTAACATTCCCCTGTAGAGTTATGTCTGGAAGCAACCTCTCCTGTCTCTTGC
 AGGGCTCCTGAGCTGAAGTGACGATGGTCACACTCAAGGAAGAACCTTCTGTCCCAGCTT
 CTTACAGCATGGAAGGTTTCTGCTTAGCGCTGACTCTTCCACAATGAAGTACTTTCT
 CAGGATCTCATTTGCTCCTGGCTCAGTGACCCTGTAGAACTGTCTCAATGGCTTTCTC
 AGTCACCCCCACTCCCTTGCCTCAGCCTTTGACCTGGAAGTTCTCAGTATTGATTCCAG
 TACCTTATGTTCTTTCTTCTCCTTCGTTCCCTTTGTTTGCA

>ENA|AM885930|AM885930.2 Ovis aries partial Ovar-DRB1 gene for MHC class
 II antigen, Ovar-DRB1*1101 allele, exon 2
 CTATCCCGTCTCTGCAGCACATTTCTTGGAGTATTCTACGAGCGAGTGTCATTTCTTCAA
 CGGGACGGAGCGGGTGCCTTCTGGACAGATACTTCTATAATGGAGAAGAGACCTTGCG
 CTTTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGCCGACGCCAA
 GTACTGGAACAGCCAGAAGGAGATCCTGGAGCGGAAGCGGGCCGCCGTGGACACGTACTG
 CAGACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGCGGGG

>ENA|AM885931|AM885931.1 Ovis aries partial Ovar-DRB1 gene for MHC class
 II antigen, Ovar-DRB1*1201 allele, exon 2
 CTATCCCGTCTCTGCAGCACATTTCTTGGAGTATCATAAGAGCGAGTGTCATTTCTTCAA
 CGGGACGGAGCGGGTGCCTTCTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCG
 CTTTCGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGCCGGAAGCCAA
 GTACTGGAACAGCCAGAAGGAGATCCTGGAGCGGAAGCGGGCCGCCGTGGACACGTACTG
 CAGACACAACCTACGGGGTCATTGAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGCGGGG

>ENA|AM885932|AM885932.1 Ovis aries partial Ovar-DRB1 gene for MHC class
 II antigen, Ovar-DRB1*0802 allele, exon 2
 CTATCCCGTCTCTGCAGCACATTTCTTGGAGTATGCTAAGAGCGAGTGTCATTTCTTCAA
 CGGGACGGAGCGGGTGCCTTCTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCG
 CTTTCGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGCCGAGCGCCGA
 GTACTGGAACAGCCAGAAGGAGCTCCTGGAGCGGAGGCGGACCGAGGTGGACACGTACTG
 CAGACACAACCTACGGGGTCTTTGAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGCGGGG

>ENA|AM885933|AM885933.1 Ovis aries partial Ovar-DRB1 gene for MHC class
 II antigen, Ovar-DRB1*1301 allele, exon 2
 CTATCCCGTCTCTGCAGCACATTTCTTGGAGTATAGTAAGAGCGAGTGTCATTTCTTCAA
 CGGGACCGAGCGGGTGCCTTCTGGACAGATACTACACTAACGGAGAAGAGAACGTGCG
 CTTTCGACAGCGACTGGGGCGAGTTCCGGGCGGTGACCGAGCTGGGGCGGCCGACGTGA
 GCAATGGAACAGCCAGAAGGACTTCTTGGAGAGCAGGAGGACCGCGGTGGACACGTACTG
 CAGACACAACCTACGGGGTCTTTGAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGCGGGG

>ENA|AY227049|AY227049.1 Ovis aries MHC class II DR beta-chain antigen binding domain (OVAR-DRB1) gene, OVAR-DRB1*GS1 allele, partial cds.
GGAGTATACTAAGAAAGAGTGTCAATTTCTTCAATGGGACGGAGCGGGTGCGGTTGCTGGA
AAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCG
GGCGGTGGCCGAGCTGGGGCGCCGAGAGCGCCGAGTACTGGAACAGCCAGAAGGAGATCCT
GGAGAGCAGGAGGACCGCGGTGGACACGTACTGCAGACACAACCTACGGGGTCATTGAGAG
TTTCAGTGTGCAGCGCGAGGT

>ENA|AY230000|AY230000.1 Ovis aries MHC class II antigen (DRB) gene, exon 2 and partial cds.
AGTATTATAGGAGCGAGTGTCAATTTCTTCAACGGGACCGAGAGGGTGCGGCTCCTGGAAA
GATACTTCCATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTTCCGGG
CAGTGACCGAGCTGGGGCGCCCCGCCGCTGAGCAATGGAACAGCCAGAAGAACATCCTGG
AGCAGAAGCGGGCCGAGGTGAACACGGTGTGCAGACACAACCTATGGGGTCTTTGAGAGTT
TCGCTGTGCAGCGCGAG

>ENA|AY248695|AY248695.2 Ovis aries MHC class II antigen beta (Ovar-DRB) gene, exon 2 and partial cds.
AGTATTATAGGAGCGAGTGTCAATTTCTTCAACGGGACCGAGAGGGTGCGGCTCCTGGAAA
GATACTTCCATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGGTTCCGGG
CAGTGAGGCGCTGGGGCGCCCCGCCGCTGAGCAATGGAACAGCCAGAAGAACATCCTGG
AGCAGAAGCGGGCCGAGGTGAACACGGTGTGCAGACACAACCTATGGGGTCTTTGAGAGTT
TCGCTGTGCAGCGCGAG

>ENA|AY307083|AY307083.1 Ovis aries MHC class II antigen (Ovar-DRB1) gene, exon 2 and partial cds.
GAGTATACTAAGAAAGAGTGTGTTTTCTTCAACGGGACGGAGCGGGTGCGGTACCTGGAC
AGATACTTCTTTAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGA
GCGGTGACCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGCTCCTG
GAGCGCAAGCGGACCACTGTGGACACGTACTGCAGACACAACCTACGGGGTTCGGT

>ENA|AY691948|AY691948.1 Ovis aries MHC class II DRB1 (Ovar-DRB1) gene, Ovar-DRB1*1203 allele, exon 2 and partial cds.
ATCCTCTCTCTGCAGCACATTTCTTGGAGTATACTAGGAAAGAGTGTCAATTTCTTCAACG
GGACGGAGCGGGTGCGGTTGCTGGAAAGATACTTCTATAATGGAGAAGAGTACGTGCGCT
TCGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGT
ACTGGAACAGCCAGAAGGACTTCTTGGAGAGCAGGAGGACCGCGGTGGACACGTACTGCA
GACACAACCTACGGGGTTCGGTGAGAGTTTCACTGTGCAGCGGCCA

>ENA|DQ659115|DQ659115.2 Ovis aries MHC class II antigen (Ovar-DRB1) mRNA, Ovar-DRB1-Q allele, partial cds.
AGAGGCTCCCGGATGGCAGCTCTGATAGTGATGCTGATGGCGCTGAGCCCTCCCCTGGCC
TGGGCCAGGAAGATCCAACCACATTTCTTGGAGTATTCTACGAGCGAGTGTCAATTTCTTC
AACGGGACGGAGCGGGTGCGGTTCTTGGACAGATACTTCTATAATGGAGAAGAGTACGTG
CGCTTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGCCAGAGCGCC
GAGCACTGGAACAGCCAGAAGGAGCTCCTGGAGCGGAGGCGGGCCGAGGTGGACACGTAC
TGCAGACACAACCTACGGGGTCATTGAGAGTTTCACTGTGCAGCGCGAGTGGAGCCTATA
GTGACTGTGTATCCTGCAAAGACCCAGCCCCTGCAGCACCACAACCTCCTGGTCTGCTCT
GTGAATGGATTCTACCCAGGCCACATTGAAGTCAGGTGGTTCCGGAACGGCCAC

>ENA|DQ659116|DQ659116.2 Ovis aries MHC class II antigen (Ovar-DRB1) mRNA, Ovar-DRB1-R allele, partial cds.
AGAGGCTCCCGGATGGCAGCTCTGATAGTGATGCTGATGGCGCTGAGCCCTCCCCTGGCC
TGGGCCAGGAAGATCCAACCACATTTCTTGGAGTATACTAAGAAAGAGTGTGTTTTCTTC
AACGGGACGGAGCGGGTGCGGTTCTTGGACAGATACTTCTATAATGGAGAAGAGTACGCG
CGCTTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGCCGAGCGCC
AAGTACTGGAACAGCCAGAAGGAGATCCTGGAGCGGAGGCGGACCGAGGTGGACACGTAC
TGCAGACACAACCTACGGGGTTCGGTGAGAGTTTCACTGTGCAGCGCGAGTGGAGCCTATA
GTGACTGTGTATCCTGCAAAGACCCAGCCCCTGCAGCACCACAACCTCCTGGTCTGCTCT
GTGAATGGATTCTACCCAGGCCACATTGAAGTCAGGTGGTTCCGGAATGGCCAC

>ENA|DQ659117|DQ659117.2 Ovis aries MHC class II antigen (Ovar-DRB1) mRNA, Ovar-DRB1-S allele, partial cds.

AGAGGCTCCCGGATGGCAGCTCTGATAGTGATGCTGATGGCGCTGAGCCCTCCCCTGGCC
TGGGCCAGGAAGATCCAACCACATTTCTTGGAGTATACTAAGAAAGAGTGTCGTTTCTCC
AACGGGACGGAGCGGGTGCGGTTCTTGGACAGATACTTCTATAATGGAGAAGAGTACGTG
CGCTTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGCCGACGCC
AAGTACTGGAACAGCCAGAAGGAGATCCTGGAGCGGAGGCGACCGAGGTGGACACGTAC
TGCAGACACAACACTACGGGGTCATTGAGAGTTTCAGTGTGCAGCGGCGAGTGGAGCCTATA
GTGACTGTGTATCCTGCAAAGACCCAGCCCCTGCAGCACCACAACCTCCTGGTCTGCTCT
GTGAATGGATTCTACCCAGGCCACATTGAAGTCAGGTGGTTCCGGAATGGCCAC

>ENA|DQ659118|DQ659118.2 Ovis aries MHC class II antigen (Ovar-DRB1)
mRNA, Ovar-DRB1-T allele, partial cds.

AGAGGCTCCCGGATGGCAGCTCTGATAGTGATGCTGATGGCGCTGAGCCCTCCCCTGGCC
TGGGCCAGGAAGATCCAACCACATTTCTTGGAGTATACTAAGAAAGAGTGTCGTTTCTTC
AACGGGACGGAGCGGGTGCGGTACCTGGACAGATACTTCTATAATGGAGAAGAGTACGTG
CGCTTCGACAACGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGCCGACGCC
AAGTACTGGAACAGCCAGAAGAGCTCCTGGAGCGGAAGCGGGCCAATGTGGACACGTAC
TGCAGACACAACACTACGGGGTCATTGAGAGTTTCAGTGTGCAGCGGCGAGTGGAGCCTATA
GTGACTGTGTATCCTGCAAAGACCCAGCCCCTGCAGCACCACAACCTCCTGGTCTGCTCT
GTGAATGGATTCTACCCAGGCCACATTGAAGTCAGGTGGTTCCGGAACGGCCAC

>ENA|DQ659119|DQ659119.2 Ovis aries MHC class II antigen (Ovar-DRB1)
mRNA, Ovar-DRB1-U allele, partial cds.

AGAGGCTCCCGGATGGCAGCTCTGATAGTGATGCTGATGGCGCTGAGCCCTCCCCTGGCC
TGGGCCAGGAAGATCCAACCACATTTCTTGGAGTATCATAAGAGCGAGTGTCGTTTCTCC
AACGGGACGGAGCGGGTGCGGTTCTTGGACAGATACTTCTATAATGGAGAAGAGTACGCG
CGCTTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGCCGACGCC
GAGTACTGGAACAGCCAGAAGGAGCTCCTGGAGCGGAGGCGGACCGAGGTGGACACGTAC
TGCAGACACAACACTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGGCGAGTGGAGCCTATA
GTGACTGTGTATCCTGCAAAGACCCAGCCCCTGCAGCACCACAACCTCCTGGTCTGCTCT
GTGAATGGATTCTACCCAGGCCACATTGAAGTCAGGTGGTTCCGGAACGGCCAC

>ENA|FJ213446|FJ213446.1 Ovis aries MHC class II antigen (DRB1) gene,
DRB1-G1 allele, exon 2 and partial cds.

GGAGTATACTAAGAAAGAGTGTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTTCTTGG
CAGATACTTCTATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGATCCT
GGAGCAGACGCGGGCCGAGGTGGACACGTACTGCAGACACAACACTACGGGGTCGGTGA

>ENA|FJ213447|FJ213447.1 Ovis aries MHC class II antigen (DRB1) gene,
DRB1-F allele, exon 2 and partial cds.

CGCTCCTGTGACCAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATGCTAAGAGC
GAGTGTCAATTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGACAGATACTTCTATAAT
GGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTG
GGGCGGCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGCTCCTGGAGCGGAGGCGGACC
GAGGTGGACACGTACTGCAGACACAACACTACGGGGTCTTTGAGAGTTTCAGTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCGGCCAG

>ENA|FJ213448|FJ213448.1 Ovis aries MHC class II antigen (DRB1) gene,
DRB1-new1 allele, exon 2 and partial cds.

GGAGTATTCTACGAGCGAGTGTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGG
CAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCG
AGCGGTGGCCGAGCTGGGGCGGCGGAGCGCCAAGTACTGGAACAGCCAGAAGGACATCCT
GGAGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACAACACTAC

>ENA|FM164421|FM164421.1 Ovis aries partial Ovar-DRB1 gene for MHC class
II antigen, Ovar-DRB1*1401 allele, exon 2

CGCTCCTGTGACCAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATACTAAGAAA
GAGTGTCAATTTCTTCAATGGGACGGAGCGGGTGCGGTTGCTGGAAAGATACTTCTATAAT
GGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTG
GGGCGGCGAGCGCCGAGTACTGGAACAGCCAGAAGGAGATCCTGGAGAGCAGGAGGACC
GCGGTGGACACGTACTGCAGACACAACACTACGGGGTCATTGAGAGTTTCAGTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCGGCCAG

>ENA|FM164422|FM164422.1 Ovis aries partial Ovar-DRB1 gene for MHC class II antigen, Ovar-DRB1*0304 allele, exon 2
CGCTCCTGTGACTAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATACTAAGAAA
GAGTGTTCGTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGACAGATACTTCTATAAT
GGAGAAGAGTACGTCGCTTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTG
GGGCGGCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGATCCTGGAGCGGAGGCGGGACC
GAGGTGGACACGTACTGCAGACACAACCTACGGGGTCATTGAGAGTTTCAGTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCGGCCAG

>ENA|FM209039|FM209039.1 Ovis aries partial Ovar-DRB1 gene for MHC class II antigen, Ovar-DRB1*1501 allele, exon 2
CGCTCCTGTGACCAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATTCTACGAGC
GAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGACAGATACTTCTATAAT
GGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTG
GGGCGGCGGAGCGCCGAGCACTGGAACAGCCAGAAGGAGCTCCTGGAGCGGAGGCGGGGCC
GAGGTGGACACGTACTGCAGACACAACCTACGGGGTCATTGAGAGTTTCAGTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCGGCCAG

>ENA|FM209040|FM209040.1 Ovis aries partial Ovar-DRB1 gene for MHC class II antigen, Ovar-DRB1*1601 allele, exon 2
CCCTCCTGTGACCAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATACTAAGAAA
GAGTGTTCGTTTCTTCAACGGGACGGAGCGGGTGCGGTACCTGGACAGATACTTCTATAAT
GGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTG
GGGCGGCCGAGCGCCAAGTACTGGAACAGCCAGAAGGAGCTCCTGGAGCGGAAGCGGGGCC
AATGTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCGGCCAG

>ENA|FM209041|FM209041.1 Ovis aries partial Ovar-DRB1 gene for MHC class II antigen, Ovar-DRB1*0702 allele, exon 2
CGCTCCTGTGACCAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATCATAAGAGC
GAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGACAGATACTTCTATAAT
GGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTG
GGGCGGCCGAGCGCCAAGTACTGGAACAGCCAGAAGGACTTCTTGGAGAGCAGGAGGACC
GCGGTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCGGCCAG

>ENA|FM209042|FM209042.1 Ovis aries partial Ovar-DRB1 gene for MHC class II antigen, Ovar-DRB1*1701 allele, exon 2
CGCTCCTGTGACCAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATGCTAAGAGA
GAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGACAGATACTTCTATAAT
GGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTG
GGGCGGCGGAGCGCCGAGTACTGGAACAGCCAGAAGGACTTCTTGGAGCGGGCGCGGGGCC
GCCGTGGACACGTACTGCAGACACAACCTACGGGGTCATTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCGGCCAG

>ENA|FN543113|FN543113.1 Ovis aries partial ovar-DRB1 gene for MHC class II antigen, allele ovar-DRB1*0101, exon 2
CGCTCCTGTGACTAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATACTAAGAAA
GAGTGTTCGTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGACAGATACTTCCATAAT
GGAGAAGAGACCCTGCGCTTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTG
GGGCGGCCGAGCGCCAAGTACTGGAACAGCCAGAAGGACTTCTTGGAGCGGGCGCGGGGCC
GCCGTGGACACGTACTGCAGACACAACCTACGGGGTCATTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCGG

>ENA|FN543114|FN543114.1 Ovis aries partial ovar-DRB1 gene for MHC class II antigen, allele ovar-DRB1*0201, exon 2
CGCTCCTGTGACTAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATTCTACGAGC
GAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGACAGATACTTCTATAAT
GGAGAAGAGACCCTGCGCTTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTG
GGGCGGCCGAGCGCCAAGTACTGGAACAGCCAGAAGGACTTCTTGGAGCAGACGCGGGGCC
GCCGTGGACACGTACTGCAGACACAACCTACGGGGTCATTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCGGTCAG

>ENA|FN543115|FN543115.1 Ovis aries partial ovar-DRB1 gene for MHC class II antigen, allele ovar-DRB1*0301, exon 2
TCTCTGCAGCACATTTCTTGGAGTATACTAAGAAAAGAGTGTCTGTTTCTCCAACGGGACGG
AGCGGGTGCGGTTCCTGGACAGATACTTCCATAATGGAGAAGAGTACGCGCGCTTCGACA
GCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGGCCGGACGCCAAGTACTGGA
ACAGCCAGAAGGAGATCCTGGAGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACA
ACTACGGGGTCATTGAGAGTTTCAGTGTGCAGCGGCGAGGTGAGCGCGGGGGTGGGCGGC
CAGTGTGGAGCAGTGTG

>ENA|FN543116|FN543116.1 Ovis aries partial ovar-DRB1 gene for MHC class II antigen, allele ovar-DRB1*0501, exon 2
CGCTCCTGTGACCAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATGCTAAGAGC
GAGTGTCTGTTTCTTCAACGGGACGGAGCGGGTGCGGTTCCTGGAAAGATACTTCTATAAT
GGAGAAGAGACCCTGCGCTTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTG
GGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGCTCCTGGAGCGGAAGCGGGCC
AATGTGGACACGTACTGCAGACACAACCTACGGGGTTCGGTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCGGCCAGTGTGGAGCAGTGTG

>ENA|FN543117|FN543117.1 Ovis aries partial ovar-DRB1 gene for MHC class II antigen, allele ovar-DRB1*0601, exon 2
ATTAGCCTCCCCCAGGAGTCCGCTCCTGTGACCAGATCTATCCCGTCTCTGCAGCACAT
TTCTTGGAGTATGCTAAGAGCGAGTGTCTGTTTCTTCAACGGGACGGAGCGGGTGCGGTTC
CTGGAAAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAG
TACCGAGCGGTGGCCGAGCTGGGGCGGGCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAC
TTCCTGGAGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACCTACGGGGTTCGGT
GAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGCGGGGGTGGGCGG

>ENA|FN543118|FN543118.1 Ovis aries partial ovar-DRB1 gene for MHC class II antigen, allele ovar-DRB1*0801, exon 2
CGCTCCTGTGACCAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATCATAAGAGC
GAGTGTCTATTTCTTCAACGGGACGGAGCGGGTGCGGTTCCTGGACAGATACTTCCATAAT
GGAGAAGAGTTCTGTGCGCTTCGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTG
GGGCGGCCGGAGCGCCGAGTACTGGAACAGCCAGAAGGAGCTCCTGGAGCGGAGGCGGACC
GAGGTGGACACGTACTGCAGACACAACCTACGGGGTCTTTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCGG

>ENA|FN543119|FN543119.1 Ovis aries partial ovar-DRB1 gene for MHC class II antigen, allele ovar-DRB1*0901,
TAGTTGGGGTGCCAGTGGAGCCAGAGAGGGGCTTAGGGCTAGTCTTGGCGGCTCCAGCGG
AGCCTGGGCGTCCACATTTGGTGGGTGTTGCCCCTGCCCTCCATCCCTCAGCCTCTCCCC
AGGAGTCCGCTCCTGTGACCAGATCTATCCTCTCTCTGCAGCACATTTCTTGGAGTATTA
TAGGAGCGAGTGTCTTTCTTCAACGGGACCGAGAGGGTGCGGCTCCTGGAAAGATACTT
CCATAATGGAGAAGAGTTTCGCGCGCTTCGACAGTGAAGTGGGGCGAGTTTCGGGCAGTGAC
CGAGCTGGGGAGGCCGCGCTGAGCAATGGAACAGCCAGAAGAACATCCTGGAGCAGAA
GCGGGCCGAGGTGAACACGGTGTGCAGACACAACCTATGGGGTCTTTGAGAGTTTCGCTGT
GCAGCGGCGAGGTGAGCGCGGGGGTGGGCTG

>ENA|FR686849|FR686849.1 Ovis aries partial ovar-DRB1 gene for MHC class II antigen, allele ovar-DRB1*2202, exon 2
CGCTCCTGTGACCAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATCATAAGAGC
GAGTGTCTATTTCTTCAACGGGACGGAGCGGGTGCGGTTCCTGGACAGATACTTCTATAAT
GGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTG
GGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGACTTCTGGAGCGGAAGCGGGCC
AATGTGGACACGTACTGCAGACACAACCTACGGGGTTCGGTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCGG

>ENA|FR686850|FR686850.1 Ovis aries partial ovar-DRB1 gene for MHC class II antigen, allele ovar-DRB1*2401, exon 2
CGCTCCTGTGACCAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATTTCTACGAGC
GAGTGTCTATTTCTTCAACGGGACGGAGCGGGTGCGGTTCCTGGACAGATACTTCTATAAT
GGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTG

GGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGACTTCCTGGAGCGGGCGCGGGCC
CCCGTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCAG

>ENA|FR686851|FR686851.1 Ovis aries partial ovar-DRB1 gene for MHC class II antigen, allele ovar-DRB1*0503, exon 2

CGCTCCTGTGACCAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATCGTAAGAGC
GAGTGTGCTTTCTTCAACGGGACGGAGCGGGTGCGGTTCCTGGAAAGATACTTCCATAAT
GGAGAAGAGACCCTGCGCTTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTG
GGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAAGAGCTCCTGGAGCGGAAGCGGGCC
AATGTGGACACGTACTGCAGACACAACCTACGGGGTCATTGAGAGTTTCAGTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCGG

>ENA|HG515540|HG515540.1 Ovis aries partial Ovar-DRB1 gene for MHC class II antigen, breed Welsh Mountain White, allele Ovar-DRB1*12:01:02, exon 2

CGCTCCTGTGACCAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATCATAAGAGC
GAGTGTGCTTTCTTCAACGGGACGGAGCGGGTGCGGTTCCTGGACAGATACTTCTATAAT
GGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTCCGGGCGGTGGCCGAGCTG
GGGCGGCCGGAAGCCAAGTACTGGAACAGCCAGAAGGAGATCCTGGAGCGGAAGCGGGCA
CCCGTGGACACGTACTGCAGACACAACCTACGGGGTCATTGAGAGTTTCAGTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCGG

>ENA|HG515541|HG515541.1 Ovis aries partial Ovar-DRB1 gene for MHC class II antigen, breed Welsh Mountain White, allele Ovar-DRB1*04:06:01, exon 2

CGCTCCTGTGACTAGATCTATCCCGTCTCTGCAGCACATTTCTTGGAGTATCATAAGAGC
GAGTGTGCTTTCTTCAACGGGACGGAGCGGGTGCGGTACCTGGACAGATACTTCCATAAT
GGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTG
GGGCGGCCGAGCGCCGAGTACTGGAACAGCCAGAAGGACTTCTTGGAGCAGACGCGGGCC
GAGGTGGACACGTACTGCAGACACAACCTACGGGGTCATTGAGAGTTTCAGTGTGCAGCGG
CGAGGTGAGCGCGGGGGTGGGCGG

>ENA|KC733419|KC733419.1 Ovis aries breed Kazak MHC class II anitgen (Ovar-DRB1) gene, Ovar-DRB1*06 allele, exon 2 and partial cds.

TATCCCGTCTCTGCAGCACATTTCTTGGAGTATGCTAAGAGCGAGTGTGCTTTCTTCAAC
GGGACGGAGCGGGTGCGGTTCCTGGAAAGATACTTCTATAATGGAGAAGAGTACGTGCGC
TTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGCGGAGCGCCGAG
TACTGGAACAGCCAGAAAGAGCTCCTGGAGCGGAAGCGGGCCAATGTGGACACGTACTGC
AGACACAACCTACGGGGTCATTGAGAGTTTCAGTGTGCAGCGGCGAGGTGAGCGC

>ENA|KC733420|KC733420.1 Ovis aries breed Kazak MHC class II anitgen (Ovar-DRB1) gene, Ovar-DRB1*07 allele, exon 2 and partial cds.

TATCCCGTCTCTGCAGCACATTTCTTGGAGTATGCTAAGAGCGAGTGTGCTTTCTTCAAC
GGGACGGAGCGGGTGCGGTTCCTGGAAAGATACTTCTATAATGGAGAAGAGTACGTGCGC
TTCGACAGCGACTGGGGCGAGTTCGGGCGGTGGCCGAGCTGGGGCGGCGGAGCGCCAG
TACTGGAACAGCCAGAAGGATTTCTTGGAGAGCAGGAGGACCGCGGTGGACACGTACTGC
AGACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGC

>ENA|KC733421|KC733421.1 Ovis aries breed Kazak MHC class II anitgen (Ovar-DRB1) gene, Ovar-DRB1*20 allele, exon 2 and partial cds.

TATCCCGTCTCTGCAGCACATTTCTTGGAGTATTATAAGGGCGAGTGTGCTTTCTTCAAC
GGGACCGAGCGGGTGCGGTTGCTGCACAGATTCTACACTAATGGAGAAGAGACCGTGCGC
TTCGACAGCGACTGGGGCGAGTTCGGGCGGTGACCCAGCAGGGGCAGGAGGACGCGGAG
CACTGGAACAGCCAGAAGGAGATCCTGGAGCGGAAGCGGGCCGAGGTGGACACGGTGTGC
AGACACAACCTATGGGGTCGGTTGAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGC

>ENA|KC733422|KC733422.1 Ovis aries breed Kazak MHC class II anitgen (Ovar-DRB1) gene, Ovar-DRB1*10 allele, exon 2 and partial cds.

TATCCCGTCTCTGCAGCACATTTCTTGGAGTATGCTAAGAGCGAGTGTGCTTTCTTCAAC
GGGACGGAGCGGGTGCGGTTCCTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCGC
TTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGCGGAGCGCCAG
TACTGGAACAGCCAGAAGGAGATCCTGGAGCGGAGGCGGACCGAGGTGGACACGTACTGC
AGACACAACCTACGGGGTCATTGAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGC

>ENA|KC733423|KC733423.1 Ovis aries breed Kazak MHC class II anitgen (Ovar-DRB1) gene, Ovar-DRB1*0701 allele, exon 2 and partial cds.
TATCCCGTCTCTGCAGCACATTTCTTGGAGTATACTAAGAAAGAGTGTCAATTTCTTCAAC
GGGACGGAGCGGGTGCGGTTTCTGGAAAGATACTTCTATAATGGAGAAGAGTACGTGCGC
TTCGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGCGAGCGCCGAG
TACTGGAACAGCCAGAAGGATTTCTTGGAGAGCAGGAGGACCGCGGTGGACACGTACTGC
AGACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGC

>ENA|KC733424|KC733424.1 Ovis aries breed Kazak and Chinese merino MHC class II anitgen (Ovar-DRB1) gene, Ovar-DRB1*1702 allele, exon 2 and partial cds.
TATCCCGTCTCTGCAGCACATTTCTTGGAGTATCATAAGAGCGAGTGTCAATTTCTTCAAC
GGGACGGAGCGGGTGCGGTTTCTTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCGC
TTCGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGCGAGCGCCGAG
TACTGGAACAGCCAGAAGGACTTCTTGGAGCGGGGCGGGGCCCGCGTGGACACGTACTGC
AGACACAACCTACGGGGTCTTTGAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGC

>ENA|KC733425|KC733425.1 Ovis aries breed Chinese merino MHC class II anitgen (Ovar-DRB1) gene, Ovar-DRB1*0101 allele, exon 2 and partial cds.
TATCCCGTCTCTGCAGCACATTTCTTGGAGTATACTAAGAAAGAGTGTCTGTTTCTTCAAC
GGGACGGAGCGGGTGCGGTTTCTTGGACAGATACTTCTATAATGGAGAAGAGACCTTGC
TTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGCGAGCGCCGAG
TACTGGAACAGCCAGAAGGACTTCTTGGAGCGGGGCGGGGCCCGCGTGGACACGTACTGC
AGACACAACCTACGGGGTCATTGAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGC

>ENA|KC733426|KC733426.1 Ovis aries breed Kazak and Chinese merino MHC class II anitgen (Ovar-DRB1) gene, Ovar-DRB1*2002 allele, exon 2 and partial cds.
TATCCCGTCTCTGCAGCACATTTCTTGGAGTATGCTAAGAGCGAGTGTCTGTTTCTTCAAC
GGGACGGAGCGGGTGCGGTTTCTTGGAAAGATACTTCTATAATGGAGAAGAGTACGTGCGC
TTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGCGAGCGCCGAG
TACTGGAACAGCCAGAAGGACTTCTTGGAGCGGAAGCGGGCCAATGTGGACACGTACTGC
AGACACAACCTACGGGGTCATTGAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGC

>ENA|KC733427|KC733427.1 Ovis aries breed Chinese merino MHC class II anitgen (Ovar-DRB1) gene, Ovar-DRB1*0301 allele, exon 2 and partial cds.
TATCCCGTCTCTGCAGCACATTTCTTGGAGTATACTAAGAAAGAGTGTCTGTTTCTTCAAC
GGGACGGAGCGGGTGCGGTTTCTTGGACAGATACTTCTATAATGGAGAAGAGTACGCGCGC
TTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGCGAGCGCCGAG
TACTGGAACAGCCAGAAGGAGATCCTTGGAGCGGAGCGGACCGAGGTGGACACGTACTGC
AGACACAACCTACGGGGTCATTGAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGC

>ENA|KC733428|KC733428.1 Ovis aries breed Chinese merino MHC class II anitgen (Ovar-DRB1) gene, Ovar-DRB1*1903 allele, exon 2 and partial cds.
TATCCCGTCTCTGCAGCACATTTCTTGGAGTATCATAAGAGCGAGTGTCAATTTCTTCAAC
GGGACGGAGCGGGTGCGGTTTCTTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCGC
TTCGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGCGAGCGCCGAG
TACTGGAACAGCCAGAAGGACTTCTTGGAGCAGACGCGGGCCGAGGTGGACACGTACTGC
AGACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGC

>ENA|KC733429|KC733429.1 Ovis aries breed Kazak MHC class II anitgen (Ovar-DRB1) gene, Ovar-DRB1*1008 allele, exon 2 and partial cds.
TATCCCGTCTCTGCAGCACATTTCTTGGAGTATTCTACGAGCGAGTGTCAATTTCTTCAAC
GGGACGGAGCGGGTGCGGTTTCTTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCGC
TTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGCGAGCGCCGAG
TACTGGAACAGCCAGAAGGAGATCCTTGGAGCGGAGCGGACCGAGGTGGACACGTACTGC
AGACACAACCTACGGGGTCTTTGAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGC

>ENA|KC733430|KC733430.1 Ovis aries breed Kazak MHC class II anitgen (Ovar-DRB1) gene, Ovar-DRB1*1502 allele, exon 2 and partial cds.
TATCCCGTCTCTGCAGCACATTTCTTGGAGTATCATAAGAGCGAGTGTCAATTTCTTCAAC
GGGACGGAGCGGGTGCGGTTTCTTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCGC
TTCGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGCGAGCGCCGAG

CACTGGAACAGCCAGAAGGAGCTCCTGGAGCGGAGGCGGGCCGAGGTGGACACGTACTGC
AGACACAACACTACGGGGTCATTGAGAGTTTTCAGTGTGCAGCGGCGAGGTGAGCGC

>ENA|KC733431|KC733431.1 Ovis aries breed Chinese merino MHC class II
anitgen (Ovar-DRB1) gene, Ovar-DRB1*1901 allele, exon 2 and partial cds.
TATCCCGTCTCTGCAGCACATTTCTTGGAGTATGCTAAGAGCGAGTGTCAATTTCTTCAAC
GGGACGGAGCGGGTGCAGTTTCTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCGC
TTTGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGCGGAGCGCCGAG
TACTGGAACAGCCAGAAGGACTTCTGGAGCAGACGCGGGCCGAGGTGGACACGTACTGC
AGACACAACACTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGGCGAGGTGAGCGC

>ENA|KC733432|KC733432.1 Ovis aries breed Kazak MHC class II anitgen
(Ovar-DRB1) gene, Ovar-DRB1*2002 allele, exon 2 and partial cds.
TATCCCGTCTCTGCAGCACATTTCTTGGAGTATGCTAAGAGCGAGTGTCTTTCTTCAAC
GGGACGGAGCGGGTGCAGTTTCTGGAAAGATACTTCTATAATGGAGAAGAGTACGTGCGC
TTTGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGCGGAGCGCCAAG
TACTGGAACAGCCAGAAGGACTTCTGGAGCGGAAGCGGGCCAATGTGGACACGTACTGC
AGACACAACACTACGGGGTCTTTGAGAGTTTTCAGTGTGCAGCGGCGAGGTGAGCGC

>ENA|KC733433|KC733433.1 Ovis aries breed Kazak MHC class II anitgen
(Ovar-DRB1) gene, Ovar-DRB1*1001 allele, exon 2 and partial cds.
TATCCCGTCTCTGCAGCACATTTCTTGGAGTATTCTACGAGCGAGTGTCAATTTCTTCAAC
GGGACGGAGCGGGTGCAGTTTCTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCGC
TTTGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGCGGAGCGCCAAG
TACTGGAACAGCCAGAAGGAGATCCTGGAGCGGAGGCGGACCGAGGTGGACACGTACTGC
AGACACAACACTACGGGGTCATTGAGAGTTTTCAGTGTGCAGCGGCGAGGTGAGCGC

>ENA|KC733434|KC733434.1 Ovis aries breed Kazak and Chinese merino MHC
class II anitgen (Ovar-DRB1) gene, Ovar-DRB1*1006 allele, exon 2 and
partial cds.
TATCCCGTCTCTGCAGCACATTTCTTGGAGTATGCTAAGAGCGAGTGTCTTTCTTCAAC
GGGACGGAGCGGGTGCAGTTTCTGGAAAGATACTTCTATAATGGAGAAGAGTACGTGCGC
TTTGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCGAGCTGGGGCGGCGGAGCGCCAAG
TACTGGAACAGCCAGAAGGAGATCCTGGAGCGGAGGCGGACCGAGGTGGACACGTACTGC
AGACACAACACTACGGGGTCATTGAGAGTTTTCAGTGTGCAGCGGCGAGGTGAGCGC

>ENA|M73984|M73984.1 Ovis aries MHC Ovar-DRB1 mRNA, complete cds.
TTTTTTTTGAGAGGACTTGCTGCTCCTCTCCCTCTCTATCCTCTGCTGTTCTCCAGCA
TGGTGTGCCTGTATTTCTCCAGAGGCTCCCGGATGGCAGCTCTGATAGTGATGCTGATGG
CGCTGAGCCCTCCCTGGCCTGGGCCAGGAAGATCCAACCACATTTCTTGGAGTATACTA
AGAAAGAGTGTCTGTTTCTCCAACGGGACGGAGCGGGTGCAGTTTCTGGACAGATACTTCT
ATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGAGCGGTGGCCG
AGCTGGGGCGGCGGACGCCAAGTACTGGAACAGCCAGAAGGAGATCCTGGAGCGGAGGC
GGACCGAGGTGGACACGTACTGCAGACACAACACTACGGGGTCGGTGAGAGTTTCACTGTGC
AGCGGCGAGTGGAGCCTATAGTGAATGCTGTATCCTGCAAAGACCCAGCCCTGCAGCACC
ACAACCTCCTGGTCTGCTCTGTGAATGGATTCTACCCAGGCCACATTGAAGTCAGGTGGT
TCCGGAATGGCCACGAAGAGGAGGCTGGGGTGATCTCCACAGGCTGATCCAGAATGGAG
ACTGGACCTTCCAGACCATGGTGATGCTTGAAACAGTTCTCAGAGTGGAGAGGTCTACA
CCTGCCAAGTGGATCACCCAGCCGGACGAGCCCTATCACAGTGGAAATGGAGGGGCACGGT
CTGACTCAGCTCAGAGCAAGATGATGAGTGGAGTTGGGGGCTTTGTTCTGGGTCTGCTCT
TCCTTGCGGTGGGGCTCTTCATCTACTTCAGGAATCAGAAAGGACGCCCTACCCCTCAGC
CAACAGGGCTCCTGAGCTGAAGTGACGATGGTCACACTCAAGGAAGAACCTTCTGTCCCA
GCTTCTTCACAGCATGGAAAGGTTTCTGCTTAGCGCTGACTCTTCCACGATGAAGTACT
TTCTCAGGATCTCATTTGCTCCTGGCTCAGTGACCCCTGTAGAACTGTCTCAATGGCTT
TCTCAGTACCCCCACTCCCTTGCCCTCAGCCTTTGACCTGGAAGTTCTCAGTATTGATT
CCAGTACCTTATGTTCTTTCTTCCTTCGTTCCCTTTGTTTGCAACTTCTGTTTCTCTGTGC
ATCTGAGCTCATCTGTTTCAATTTTACTTTATAATGTGTTCCCTCAAATAAATACGGAGTGA
AAATC

>ENA|M93432|M93432.1 Merino MHC OVAR-DRB1.2 chain (MHC OVAR-DRB1) mRNA,
complete cds.
CTCCAGCATGGTGTGCTGTATTTCTCCAGAGGCTCCCGGATGGCAGCTCTGATAGTGAT
GCTGATGGCGCTGAGCCCTCCCTGGCCTGGGCCAGGAAGATCCAACCACATTTCTGGA

GTATACTAAGAAAGAGTGTCAATTTCTTCAACGGGACGGAGCGGGTGCGGTTGCTGGAAAG
 ATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCGGGC
 GGTGGCCGAGCTGGGGCGGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGATTTCTTGGAG
 GAGCAGGAGGACCGCGGTGGACACGTACTGCAGACACAACACTACGGGGTTCGGTGAGAGTTT
 CACTGTGCAGCGGCGAGTGGAGCCTACTGTGACTGTGTATCCTGCAAAGACCCAGCCCCCT
 GCAGCACCACAACCTCCTGGTCTGCTCTGTGAATGGATTCTACCCAGGCCACATTGAAGT
 CAGGTGGTTCCGGAACGGCCACGAAGAGGAGGCTGGGGTGATCTCCACAGGCCGTGATCCA
 GAATGGAGACTGGACCTTCCAGACCATGGTGATGCTTGAAAACAGTTCTTCAGAGTGGAGA
 GGTCTACACCTGCCAAGTGGATCACCCAGCCGGACGAGCCCTATCACAGTGGAAATGGAG
 GGCACGGTCTGACTCAGCTCAGAGCAAGATGATGAGTGGAGTTGGGGGCTTTGTTCTGGG
 TCTGCTCTTCCTTGCGGTGGGGCTCTTCATCTACTTCAGGAATCAGAAAGGACGCCCTAC
 CCTTCAGCCAACAGGGCTCCTGAGCTGAAGTGACGATGGTCACACTCAAGGAAGAACCTT
 CTGTCCCAGCTTCTTCACAGCATGGAAAGGTTTCTGCTTAGCGCTGACTCTTCCACGAT
 GAAGTACTTTCTCAGGATCTCATTTGCTCCTGGCTCAGTGACCCTGTAGAAACTGTCTC
 AATGGCTTCTCAGTCACCCCACTCCCTTGCCCTCAGCCTTGACCTGGAAGTTCTCAGTAT
 TGATTCCAGTACCTTATGTTCTTTCTTCTCGTTCCCTTTGTTTGCAACTTCTGTTTCC
 TGTGCATCTGAGCTCATCTGTTTACTTTTATAATGTGTTCCCTCAAATAAATACGG
 AGTGAAAATCA

>ENA|U00204|U00204.1 *Ovis aries* Perendale and Romney breeds DR beta-chain
 antigen binding domain, MHC class II DRB (Ovar-DRB01) gene, partial cds.
 AGTATACTAAGAAAGAGTGTGTTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGACA
 GATACTTCCATAATGGAGAAGAGACCCTGCGCTTCGACAGCGACTGGGGCGAGTACCGAG
 CGGTGGCCGAGCTGGGGCGGCCGGACGCTAAGTACTGGAACAGCCAGAAGGACTTCTTGG
 AGCGGGCGCGGGCCCGCGTGGACACGTACTGCAGACACAACACTACGGGGTCATTGAGAGTT
 TCACTGTGCAGCGCGAGGTGAGCGCGGGGTGGGCGGCCACTGTGGAGCAGTGTGTGTG
 TG
 AG
 AG
 AGA

>ENA|U00205|U00205.1 *Ovis aries* subspecies Argali DR beta-chain antigen
 binding domain, MHC class II DRB (Ovar-DRB02) gene, partial cds.
 AGTATACTAAGAAAGAGTGTGTTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGACA
 GATACTTCCATAATGGAGAAGAGACCCTGCGCTTCGACAGCGACTGGGGCGAGTACCGAG
 CGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGACTTCTTGG
 AGCGGGCGCGGGCCACCGTGGACACGTACTGCAGACACAACACTACGGGGTCATTGAGAGTT
 TCACTGTGCAGCGCGAGGTGAGCGCGGGGTGGGCGGCCACTGTGGAGCAGTGTGTGTG
 TG
 AG
 AG
 AG

>ENA|U00206|U00206.1 *Ovis aries* Perendale and Texel breeds DR beta-chain
 antigen binding domain, MHC class II DRB (Ovar-DRB04) gene, partial cds.
 AGTATACTAAGAAAGAGTGTGTTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGACA
 GATACTTCCATAATGGAGAAGAGACCCTGCGCTTCGACAGCGACTGGGGCGAGTACCGAG
 CGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGACTTCTTGG
 AGCGGGCGCGGGCCCGCGTGGACACGTACTGCAGACACAACACTACGGGGTTCGGTGAGAGTT
 TCAGTGTGCAGCGCGAGGTGAGCGCGGGGTGGGCGGCCAGTGTGGAGCAGTGTGTGTG
 TG
 AG
 CGAG
 CAG

>ENA|U00207|U00207.1 *Ovis aries* subspecies Argali DR beta-chain antigen
 binding domain, MHC class II DRB (Ovar-DRB05) gene, partial cds.
 AGTATACTAAGAAAGAGTGTGTTTTCTTCAACGGGACGGAGCGGGTGCGGTTCTTGGACA
 GATACTTCCATAATGGAGAAGAGACCCTGCGCTTCGACAGCGACTGGGGCGAGTACCGAG
 CGGTGGCCGAGCTGGGGCGGCCGGACGCCGAGTACTGGAACAGCCAGAAGGACTTCTTGG
 AGCGGGCGCGGGCCCGCGTGGACACGTACTGCAGACACAACACTACGGGGTTCGGTGAGAGTT
 TCAGTGTGCAGCGCGAGGTGAGCGCGGGGTGGGCGGCCAGTGTGGAGCAGTGTGTGTG
 TG
 AG
 AG
 AG

>ENA|U00208|U00208.1 *Ovis aries* Finnish Landrace breed DR beta-chain antigen binding domain, MHC class II DRB (Ovar-DRB06) gene, partial cds.

AGTATACTAAGAAAGAGTGTCTGTTTCTCCAACGGGACGGAGCGGGTGCGGTTCCTGGACA
GATACTTCTATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGAG
CGGTGGCCGAGCTGGGGCGGCCGGACGCCGAGTACTGGAACAGCCAGAAGGAGATCCTGG
AGCAGACGCGGGCCGCCGTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGAGAGTT
TCACTGTGCAGCGCGAGGTGAGCGCGGGGTGGGCGGCCACTGTGGAGCAGTGTGTGTG
TGTGTGTGTGTGTGTGTGTGAG
AGAGAGAGAGCGCGCGAGAGAGAGAGAGCGCGCGAGAGCGAGAGCGAGAGCGACAGAGAGAG
ACAGAGAGAGTGGGAGAGAGAGAGACAGACAGAGAGAGACAGACAGA

TGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGAGAGAGAGAGAGAG
AGAGAGAGAGAGAGCGCGAGAGCGAGAGCGAGAGCGAGAGCGGACAGAGAGAGACAGAGAG
CGTGGGAGAGAGAGAGACAGACAGAGACAGACAGA

>ENA|U00226|U00226.1 Ovis aries Merino breed DR beta-chain antigen binding domain, MHC class II DRB (Ovar-DRB23) gene, partial cds.

AGTATCATAAGAGCGAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCCCTGGACA
GATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCGAG
CGGTGGCCGAGCTGGGGCGGCAGAGCGCCGAGCACTGGAACAGCCAGAAGGAGCTCCTGG
AGCGGAGGCGGGCCGAGGTGGACACGTACTGCAGACACAACACTACGGGGTCATTGAGAGTT
TCAGTGTGCAGCGGCGAGGTGAGCGCGGGGGTGGGCGGCCAGTGTGGAGCAGTGTGTGCG
TGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGAGAGAGAGAGAGAG
AGAGAGAGAGAGAGAGAGCGCGAGAGCGAGAGCGAGAGCGAGAGCGAGAGCGACAGAGAGAGACAG
AGAGAGTGGGAGAGAGAGACAGACAGAGACAGACAGA

>ENA|U00227|U00227.1 Ovis aries Merino breed DR beta-chain antigen binding domain, MHC class II DRB (Ovar-DRB24) gene, partial cds.

AGTATCATAAGAGCGAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCCCTGGACA
GATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTTCCGGG
CGGTGGCCGAGCTGGGGCGGCAGAGCGCCGAGTACTGGAACAGCCAGAAGGACTTCCTGG
AGCGGGCGCGGGCCCGTGGACACGTACTGCAGACACAACACTACGGGGTCTTTGAGAGTT
TCAGTGTGCAGCGGCGAGGTGAGCGCGGGGGTGGGCGGCCAGTGTGGAGCAGTGTGTGCG
TGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGAGAGAGAGAGAG
AGAGAGAGAGAGCGCGAGAGCGAGAGCGAGAGCGAGAGCGAGAGCGACAGAGAGAGACAGAGAGAG
TGGGAGAGAGAGAGACAGACAGAGACAGACAGA

>ENA|U00228|U00228.1 Ovis aries Finnish Landrace breed DR beta-chain antigen binding domain, MHC class II DRB (Ovar-DRB25) gene, partial cds.

AGTATCATAAGAGCGAGTGTTCATTTCTTCAACGGGACGGAGCGGGTGCGGTTCCCTGGACA
GATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGAG
CGGTGGCCGAGCTGGGGCGGCCGACGCCAAGTACTGGAACAGCCAGAAGGACTTCCTGG
AGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACACTACGGGGTCGGTGAGAGTT
TCACTGTGCAGCGGCGAGGTGAGCGCGGGGGTGGGCGGCCAGTGTGGAGCAGTGTGTGCG
TGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGAGAGAGAG
AGAGAGCGCGAGAGCGAGAGCGACAGAGAGAGACAGAGAGAGTGGGAGAGAGAGAGACAG
ACAGAGACAGACAGG

>ENA|U00229|U00229.1 Ovis aries Coopworth breed DR beta-chain antigen binding domain, MHC class II DRB (Ovar-DRB26) gene, partial cds.

AGTATCATAAGAGCGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTACCTGGACA
GATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGAG
CGGTGGCCGAGCTGGGGCGGCCGACGCCGAGTACTGGAACAGCCAGAAGGACTTCCTGG
AGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACACTACGGGGTCGGTGAGAGTT
TCACTGTGCAGCGGCGAGGTGAGCGCGGGGGTGGGCGGCCAGTGTGGAGCAGTGTGTGCG
TGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGAGAGAGAG
AGAGAGAGCGCGAGAGCGAGAGCGACAGAGAGAGACAGAGAGAGTGGGAGAGAGAGAGAC
AGACAGAGACAGACAGG

>ENA|U00230|U00230.1 Ovis aries Kasach DR beta-chain antigen binding domain, MHC class II DRB (Ovar-DRB27) gene, partial cds.

AGTATCATAAGAGCGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTACCTGGACA
GATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTTCCGGG
CGGTGGCCGAGCTGGGGCGGCCGACGCCGAGTACTGGAACAGCCAGAAGGACTTCCTGG
AGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACACTACGGGGTCATTGAGAGTT
TCAGTGTGCAGCGGCGAGGTGAGCGCGGGGGTGGGCGGCCAGTGTGGAGCAGTGTGTGCG
TGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGCGTGTGAGAGAGAGAGAGCG
CGAGAGCGAGAGCGAGAGCGAGAGCGACAGAGAGAGACAGAGAGAGTGGGAGAGAGAGAGAG
ACAGACAGAGACAGACAGG

>ENA|U00231|U00231.1 Ovis aries Merino breed DR beta-chain antigen binding domain, MHC class II DRB (Ovar-DRB28) gene, partial cds.

AGTATCATAAGAGCGAGTGTTCGTTTCTCCAACGGGACGGAGCGGGTGCGGTACCTGGACA
GATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCGAG

[illegible]

>ENA|U00233|U00233.1 Ovis aries Merino breed DR beta-chain antigen binding domain, MHC class II DRB (Ovar-DRB30) gene, partial cds.

AGTATCGTAAGAGCGAGTGTGCTTTCTCCAACGGGACGGAGCGGGTGCGGTACCTGGACA
GATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGAG
CGGTGGCCGAGCTGGGGCGGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGCTCCTGG
AGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACACTACGGGGTCATTGAGAGTT
TCAGTGTGCAGCGGCGAGGTGAGCGCGGGGGTGGGCGGCCAGTGTGGAGCAGTGTGTGTG
TGT
CGCGAGAGCGAGAGCGAGAGCGACAGAGAGAGACAGAGAGAGTGGGAGAGAGAGAGACAG
ACAGAGAGAGACAGACAGA

>ENA|U00235|U00235.1 *Ovis aries* subspecies Mufflon DR beta-chain antigen binding domain, MHC class II DRB (Ovar-DRB32) gene, partial cds.

AGTATAGTAAGAGCGAGTGTCAATTTCTTCAACGGGACGGAGCGGGTGCGGTTCCTGGACA
GATACTACACTAACGGAGAAGAGAACGTGCGCTTCGACAGCGACTGGGGCGAGTTCGGG
CGGTGACCGAGCTGGGGCGGCCGGACGCTGAGCAATGGAACAGCCAGAAGGACTTCCTGG
AACGGAAGCGGACCGCGGTGGACACGTACTGCAGACACAACCTACGGGGTCATTGAGAGTT
TCAGTGTGCAGCGCGAGGTGAGCGCGGGGGTGGGCAGCCAGTGTGGAGCAGTGTGTGTG
TGT
CGAGAGCGACAGAGAGAGACAGAGAGAGTGGGAGAGAGAGAGACAGACAGAGAGAGACAG
ACAGA

>ENA|U00237|U00237.1 *Ovis aries* subspecies *Argali* DR beta-chain antigen binding domain, MHC class II DRB (Ovar-DRB34) gene, partial cds.

>ENA|Z92733|Z92733.1 *Ovis aries* DNA for MHC class II DRB exon 2
AGTATCATAAGAGCGAGTGTCTGTTTCTCCAACGGGACGGAGCGGGTGCGGTTCCTGGACA
GATACTTCTATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGAG
CGGTGGCCGAGCTGGGGCGGCCGGACGCCGAGTACTGGAACAGCCAGAAGGAGCTCCTGG
ACCGGAGGCGGACCCGAGGTGGACACGTA CTGCAGACACAAC TACGGGGTCTTTGAGAGTT
TCAAGTCTGCGAGCCGCGAGGTGA

>ENA|Z92734|Z92734.1 Ovis aries DNA for MHC class II DRB exon 2
AGTATCGTAAGAGCGAGTGTCTGTTTCTCCAACGGGACGGAGCGGGTGCGGTACCTGGACA
GATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAACGACTGGGGCGAGTACCGAG
CGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGACTTCCTGG
AGCGGAAGCGGGCCAATGTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGAGAGTT
TCACTGTGCAGCGGCGAGGTGA

>ENA|Z92735|Z92735.1 Ovis aries DNA for MHC class II DRB exon 2
AGTATCATAAGAGCGAGTGTCTGTTTCTCCAACGGGACGGAGCGGGTGCGGTTCCTGGACA
GATACTTCTATAATGGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGAG
CGGTGGCCGAGCTGGGGCGGCCGGACGCCGAGTACTGGAACAGCCAGAAGGAGCTCCTGG
AGCGGAGGCGGACCGAGGTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGAGAGTT
TCACTGTGCAGCGGCGAGGTGA

Cattle

>ENA|HM031388|HM031388.1 Bos indicus MHC class II antigen DR beta chain
(BoLA-DRB3) gene, BoLA-DRB3*5702 allele, exon 2 and partial cds.
CACATTTCTGAGTATCATAAGAGTGAGTGTCTTTCTTCAACGGGACCGAGCGTTTGC
GGTACCTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGG
GCGAGTACCGGGCGGTGACCGAGCTGGGGCGGCCGGACGCCAAGTACTGGAACAGCCAGA
AGGAGATCCTGGAGCGGAGGCGGGCCGAGGTGGACACGCTGTGCAGACACAACCTACGGGG
TCGGTGAGAGTTTCACTGTGCAGCG

>ENA|HM031389|HM031389.1 Bos indicus MHC class II antigen DR beta chain
(BoLA-DRB3) gene, BoLA-DRB3*2503 allele, exon 2 and partial cds.
CACATTTCTGAGTATTCTACGAGCGAGTGTCTTTCTTCAACGGGACCGAGCGGGTGC
GGTACCTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCGCTTCGACAGCGACTGGG
GCGAGTTCCAGGCGGTGACCGAGCTGGGGCGGCCGGCCGCGCCGAGCAGTGAACAGCCAGA
AGGACACCCTGGAGGACGAGCGGGCTTCGGTGGACACGTACTGCAGATACAACCTACGGGG
TCGGTGAGAGTTTCACTGTG

>ENA|DQ834889|DQ834889.1 Bos indicus genotype HaeIII-a MHC class II
antigen (BoLa-DRB3) gene, exon 2 and partial cds.
ATCCTCTCTCTGCAGCACATTTCTGAGTATTGTAAGAGAGAGTGTCAATTTCTTCAACG
GGACCGAGCGGGTGCGGTGCTGGACAGATACTTCTATAATGGAGAAGAGCGCGTGCGCT
TCGACAGCGACTGGGGCGAGTTCCGGGCGGTGACCGAGCTGGGGCGGCCGGACGCCGAGT
ACTGGAACAGCCAGAAGGACTTCCTGGAGCAGAGGCGGGCCGCGGTGGACACGTACTGCA
GACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|DQ834890|DQ834890.1 Bos indicus genotype HaeIII-b MHC class II
antigen (BoLa-DRB3) gene, exon 2 and partial cds.
ATCCTCTCTCTGCAGCACATTTCTGAGTATTCTACGAACGAGTGTCAATTTCTTCAACG
GGACCGAGCGGGTGCGGTACCTGGACAGATACTTCCATAATGGAGAAGAGTTTCGTGCGCT
TCGACAGCGACTGGGGCGAGTACCGGGCGGTGACCGAGCTAGGGCGGCGGGACGCCGAGT
ACTGGAACAGCCAGAAGGACACCCTGGAGCGGGAGCGGGCCTATGTGGACACGTACTGCA
GACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|DQ834891|DQ834891.1 Bos indicus genotype HaeIII-d MHC class II
antigen (BoLa-DRB3) gene, exon 2 and partial cds.
ATCCTCTCTCTGCAGCACATTTCTGAGTATTCTACGAGCGAGTGTCAATTTCTTCAACG
GGACCGAGCGGGTGCGGTACCTGGACAGATACTTCCATAATGGAGAAGAGTTTCGTGCGCT
TCGACAGCGACTGGGGCGAGTACCGGGCGGTGACCGAGCTAGGGCGGCGGGTCGCCGAGC
AGTTGAACGGCCAGAAGGACACCCTGGAGCGGGAGCGGGCCTATGTGGACACGTACTGCA
GACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGGCGCGA

>ENA|DQ834892|DQ834892.1 Bos indicus genotype HaeIII-e MHC class II
antigen (BoLa-DRB3) gene, exon 2 and partial cds.
ATCCTCTCTCTGCAGCACATTTCTGAGTATTCCAAGAACGAGTGTCAATTTCTTCAACG
GGACCGAGCGGGTGCGGTTCCTGGACAGATACTTCCATAATGGAGAAGAGTTTCGTGCGCT
TCGACAGCGACTGGGGCGAGGACCGGGCGGTGACCGAGCTAGGGCGGCGGGTCGCCGAGT
ACTGGAACAGCCAGAAGGACTTCCTGGAGGAGAAGCGTGTCTATGTGGACACGTACTGCA
GACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|DQ834893|DQ834893.1 Bos indicus genotype HaeIII-f MHC class II antigen (BoLa-DRB3) gene, exon 2 and partial cds.
ATCCTCTCTTTGCAGCACATTTCTGAGTATTCTAAGAGCGAGTGTCATTTCTTCAACG
GGACCGAGCGGGTGCGGTTCTGAGAGATACTTCCATAATGGAGAAGAGAACGTGCGCT
TCGACAGCGACTGGGGCGAGTTCCGGGCGGTGACCGAGCTGGGGCGGCCGCGCCGAGT
ACTGGAACAGCCAGAAGGACATCCTGAGCGGGAGCGGGCCTATGTGGACACGTACTGCA
GACACAACACTACGGGGTCGTTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|DQ834894|DQ834894.1 Bos indicus genotype RsaI-g MHC class II antigen (BoLa-DRB3) gene, exon 2 and partial cds.
ATCCTCTCTTTGCAGCACATTTCTGAGTATTTTAAGAGCGAGTGTCATTTCTTCAACG
GGACCGAGCGGGTGCGGTTCTGAGAGATCCTTCTATAATGGAGAAGAGAACGTGCGCT
TCGACAGCGACTGGGGCGAGTACCGGGCGGTGACCGAGCTAGGGCGGCCGACGCCGAGT
ACTGGAACAGCCAGAAGGAGATCCTGAGGAGAAGCGGGCCGATGTGGACAGGGTGTGCA
GACACAACACTACGGGGTCGGGGAGAGTTTCACTGTGCAGCGGCGA

>ENA|DQ834895|DQ834895.1 Bos indicus genotype RsaI-o MHC class II antigen (BoLa-DRB3) gene, exon 2 and partial cds.
ATCCTCTCTTTGCAGCACATTTCTGAGTATTATAAGGGCGAGTGTCATTTCTTCAACG
GGACCGAGCGGGTGCGGTTCTGAGAGACACTTCTATAATGGAGAAGAGTTCGTGCGCT
TCGACAGCGACTGGGGCGAGTTCCGGGCGGTGACCGAGCTGGGGCGGCCGCGCCGAGC
ACTGGAACAGCCAGAAGGACTTCTGAGCGGAAGCGGGCCGAGGTGGACAGGGTGTGCA
GACACAACACTACGGGGTCGTTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|DQ834896|DQ834896.1 Bos indicus genotype RsaI-v MHC class II antigen (BoLa-DRB3) gene, exon 2 and partial cds.
ATCCTCTCTCTGCAGCACATTTCTGAGTATTCTACGAACGAGTGTCATTTCTTCAACG
GGACCGAGCGGGTGCGGTACCTGGACAGATACTTCCATAATGGAGAAGAGTTCGTGCGCT
TCGACAGCGACTGGGGCGAGTACCGGGCGGTGACCGAGCTAGGGCGGCCGACGCCGAGT
ACTGGAACAGCCAGAAGGACACCCTGAGCGGGAGCGGGCCTATGTGGACACGTACTGCA
GACACAACACTACGGGGTCGTTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|DQ834897|DQ834897.1 Bos indicus genotype RsaI-f MHC class II antigen (BoLa-DRB3) gene, exon 2 and partial cds.
ATCCTCTCTCTGCAGCACATTTCTGAGTATTCCAAGAGCGAGTGTCATTTCTTCAACG
GGACCGAGCGGGTGCGGTTCTGAGAGATACTTCCATAATGGAGAAGAGTTCGTGCGCT
TCGACAGCGACTGGGGCGAGTACCGGGCGGTGACCGAGCTAGGGCGGCCGACGCCGAGT
ACTGGAACAGCCAGAAGGACTTCTGAGCGGAAGCGGGCCTATGTGGACACGTACTGCA
GACACAACACTACGGGGTCGGGGAGAGTTTCACTGTGCAGCGGCGA

>ENA|DQ834898|DQ834898.1 Bos indicus genotype RsaI-i MHC class II antigen (BoLa-DRB3) gene, exon 2 and partial cds.
ATCTCTCTCTCGCAGCACATTTCTGAGTATCATAAGGGCGAGTGTCATTTCTTCAACG
GGACCGAGCGGGTGCGGTTCTGAGAGACACTTCTATAATGGAGAAGAGTTCGTGCGCT
TCGACAGCGACTGGGGCGAGTTCCGGGCGGTGACCGAGCTGGGGCGGCCGACGCCGAGT
ACTGGAACAGCCAGAAGGACTTCTGAGCGGAAGCGGGCCGAGGTGGACACGTACTGCA
GACACAACACTACGGGGTCGTGGAGAGTTTCACTGTGCAGCGGCGA

>ENA|DQ834899|DQ834899.1 Bos indicus genotype RsaI-j MHC class II antigen (BoLa-DRB3) gene, exon 2 and partial cds.
ATCCTCTCTTTGCAGCACATTTCTGAGTATTCTACGAGCGAGTGTCATTTCTTCAACG
GGACCGAGCGGGTGCGGTACCTGGACAGATACTTCCATAATGGAGAAGAGTTCGTGCGCT
TCGACAGCGACTGGGGCGAGTACCGGGCGGTGACCGAGCTAGGGCGGCCGCGGTCGCCGAGC
AGTTGAACGCCAGAAGGACACCCTGAGCAGGAGCGGGCCTATGTGGACACGTACTGCA
GACACAACACTACGGGGTCGTTGAGAGTTTCACTGTGCAGGCGCGA

>ENA|DQ834900|DQ834900.1 Bos indicus genotype RsaI-l MHC class II antigen (BoLa-DRB3) gene, exon 2 and partial cds.
ATCCTCTCTCTGCAGCACATTTCTGAGTATTCTACGAGCGAGTGTCATTTCTTCAACG
GGACCGAGCGGGTGCGGTTCTGAGAGATACTTCCATAATGGAGAAGAGTTCGTGCGCT
TCGACAGCGACTGGGGCGAGTTCCGGGCGGTGACCGAGCTAGGGCGGCCGCGGTCGCCGAGC
ATTGGAACGCCAGAAGGACACCCTGAGCGGGAGCGGGCCTATGTGGACACGTACTGCA
GACACAACACTACGGGGTCGTTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|DQ834901|DQ834901.1 Bos indicus genotype BstYI-o MHC class II antigen (BoLa-DRB3) gene, exon 2 and partial cds.
ATCCTCTCTCTGCAGCACATTTCTGAGTATTTTACGAGCGAGTGTCAATTTCTTCAACG
GGACCGAGCGGGTGCAGTACCTGGACAGATACTTCCATAATGGAGAAGAGTTCGTGCGCT
TCGACAGCGACTGGGGCGAGTACCGGGCGGTGACCGAGCTAGGGCGGCGGGTCGCCGAGC
AGTTGAACGCCAGAAGGACACCCTGGAGCGGGAGCGGGCCTATGTGGACACGTACTGCA
GACACAACCTACGGGGTCGTTGAGAGTTTCACTGTGCAGGCGCGA

>ENA|DQ834902|DQ834902.1 Bos indicus genotype BstYI-e MHC class II antigen (BoLa-DRB3) gene, exon 2 and partial cds.
ATCCTCTCTTTGCAGCACATTTCTGAGTATTTTAAGAGCGAGTGTCAATTTCTTCAACG
GGACCGAGCGGGTGCAGTTCCTGGAGAGATCCTTCTATAATGGAGAAGAGAACGTGCGCT
TCGACAGCGACTGGGGCGAGTACCGGGCGGTGACCGAGCTAGGGCGGCGCGGACGCCGAGT
ACTGGAACAGCCAGAAGGAGATCCTGGAGGAGAAGCGGGCCGATGTGGACAGGGTGTGCA
GACACAACCTACGGGGTCGGGGAGAGTTTCACTGTGCAGCGGCGA

>ENA|DQ834903|DQ834903.1 Bos indicus genotype BstYI-d MHC class II antigen (BoLa-DRB3) gene, exon 2 and partial cds.
ATCCTCTCTCTGCAGCACATTTCTGAGTATTTCAAGAAAGAGTGTCAATTTCTTCAACG
GGACCGAGCGGGTGCAGTTCCTGGACAGATCCTTCCATAATGGAGAAGAGATCGTGCGCT
TCGACAGCGACTGGGGCGAGTACCGGGCGGTGACCGAGCTAGGGCGGCGCGGACGCCGAGT
ACTGGAACAGCCAGAAGGACTTCTGGAGGAGAAGCGGGCCGCGGTGGACAGGTACTGCA
GACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|JX274225|JX274225.1 Bos indicus x Bos taurus isolate Animal42 MHC class II antigen (DRB3) gene, DRB3*1701 allele, partial cds.
CGCTCCTGTGATCAGATCTATCCTCTCTCTGCAGCACATTTCTGAGTATGCTACGAGC
GAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCAGTTCCTGCACAGATACTTCTATAAT
GGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTCCGGGCGGTGACCGAGCTG
GGGCGGCCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGATCCTGGAGCGGGAGCGGGCC
TATGTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTG

>ENA|JX274226|JX274226.1 Bos indicus x Bos taurus isolate Animal126 MHC class II antigen (DRB3) gene, DRB3*0201 allele, partial cds.
CGCTCCTGYGATCAGATCTATCCTCTCTCTGCAGCACATTTCTGAGTATTTCTACGAGC
GAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCAGTTCCTGGACAGATACTTCCATAAT
GGAGAAGAGTTCTGTCGCTTCGACAGCGACTGGGGCGAGTACCGGGCGGTGACCGAGCTA
GGGCGGCCCGGACGCCGAGTACTGGAACAGCCAGGAGATCCTGGAGCGGGCGGCGGGCGG
GTGGACACGTACTGCAGACACAACCTACGGGGCGGTGGAGAGTTTCACTGTGCAGCGGCGA
GGTGAGCGCGGGGGTG

>ENA|JX274227|JX274227.1 Bos indicus x Bos taurus isolate Animal131 MHC class II antigen (DRB3) gene, DRB3*1601 allele, partial cds.
CGCTCCTGTGATCAGATCTATCCTCTCTCTGCAGCACATTTCTGAGTATACCAAGAAA
GAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCAGTTCCTGGACAGATACTTCCATAAT
GGAGAAGAGTTCTGTGCGCTTCGATAGCGACTGGGGCGAGTACCGGGCGGTGACCGAGCTA
GGGCGGCCCGGACGCCAAGTACTGGAACAGCCAGAAGGACTTCTGGAGGAGAAGCGGGCC
CGGGTGGACACGTACTGCAGACACAACCTACGGGGTCGTTAGATTGCG

>ENA|JX274228|JX274228.1 Bos indicus x Bos taurus isolate Animal204 MHC class II antigen (DRB3) gene, DRB3*1101 allele, partial cds.
CGCTCCTGTGATCAGATCTATCCTGTCTCTGCAGCACATTTCTGCAGTATCATAAGGGC
GAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCAGTTCCTGGACAGACACTTCTATAAT
GGAGAAGAGTTCTGTCGCTTCGACAGCGACTGGGACGAGTCCGGGCGGTGACCGAGCTG
GGGCGGCCCGTCCGCCGAGTACTGGAACAGCCAGAAGGACTTCTGGAGCGGGCGGCGGGCC
GAGGTGGACACGGTGTGCAGACACAACCTACGGGGTCGTTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTG

>ENA|JX274229|JX274229.1 Bos indicus x Bos taurus isolate Animal239 MHC class II antigen (DRB3) gene, DRB3*1701 allele, partial cds.
CGCTCCTGYGATCAGATCTATCCTCTCTCTGCAGCACATTTCTGAGTATGCTACGAGC

GAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCGGTTCTGCACAGATACTTCTATAAT
GGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTTCGGGGCGGTGACCGAGCTG
GGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGATCCTGGAGCGGGAGCGGGCC
TATGTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTG

>ENA|JX274230|JX274230.1 Bos indicus x Bos taurus isolate Animal279 MHC
class II antigen (DRB3) gene, DRB3*1601 allele, partial cds.
CGCTCCTGTGATCAGATCTATCCTCTCTCTGCAGCACATTTCTGGAGTATACTAAGAAA
GAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCGGTTCTTGACAGATACTTCCATAAT
GGAGAAGAGTTCTGTCGCTTCGATAGCGACTGGGGCGAGTACGGGGCGGTGACCGAGCTA
GGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGACTTCTGGAGGAGAGCGGGCC
GCGGTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTG

>ENA|JX274231|JX274231.1 Bos indicus x Bos taurus isolate Animal304 MHC
class II antigen (DRB3) gene, DRB3*0801 allele, partial cds.
CGCTCCTGTGATCAGATCTATCCTCTCTCTGCAGCACATTTCTGGAGTATGCTACGAGC
GAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCGGTTCTTGACAGATACTTCCATAAT
GGAGAAGAGTTCGTGTCGCTTCGACAGCGACTGGGGCGAGTTCGGGGCGGTGACCGAGCTG
GGGCGGCCGTCCGCCGTGCACCTGAACAGCCAGAAGGACTTCTGGAGGACGAGCGGGCT
TCGGTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTG

>ENA|JX274232|JX274232.1 Bos indicus x Bos taurus isolate Animal407 MHC
class II antigen (DRB3) gene, DRB3*1101 allele, partial cds.
CGCTCCTGTGAYCAGATCTATCCTGTCTCTGCAGCACATTTCTGCAGTATCATAAGGGC
GAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCGGTTGCTGGACAGACACTTCTATAAT
GGAGAAGAGTACGTGTCGCTTCGACAGCGACTGGGACGAGTTCGGGGCGGTGACCGAGCTG
GGGCGGCCGTCCGCCGAGTACTGGAACAGCCAGAAGGACTTCTGGAGCGGAGCGGGCC
GAGGTGGACACGGTGTGCAGACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTG

>ENA|JX274233|JX274233.1 Bos indicus x Bos taurus isolate Animal464 MHC
class II antigen (DRB3) gene, DRB3*3601 allele, partial cds.
CGCTCCTGTGATCAGATCTATCCTGTCTCTGCAGCACATTTCTGGAGTATTCTAAGAGC
GAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCGGTTCTTGACAGATACTACACTAAT
GGAGAAGAGACCGTTCGCTTCGACAGCGACTGGGGCGAGTTCGGGGCGTTGACCGAGCTG
GGGCGGCAGGACGCCGAGTGAACAGCCAGAAGGACACCCCTGGAGCGGGAGCGGGCC
TATGTGGACACGTACTGCAGACACAACCTACGGGGCGTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTG

>ENA|JX274234|JX274234.1 Bos indicus x Bos taurus isolate Animal474 MHC
class II antigen (DRB3) gene, DRB3*1701 allele, partial cds.
CGCTCCTGTGATCAGATCTATCCTCTCTCTGCAGCACATTTCTGGAGTATGCTACGAGC
GAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCGGTTCTTGACAGATACTTCTATAAT
GGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTTCGGGGCGGTGACCGAGCTG
GGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGATCCTGGAGCGGGAGCGGGCC
TATGTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTG

>ENA|JX274235|JX274235.1 Bos indicus x Bos taurus isolate Animal500 MHC
class II antigen (DRB3) gene, DRB3*1701 allele, partial cds.
CGCTCCTGTGATCAGATCTATCCTCTCTCTGCAGCACATTTCTGGAGTATGCTACGAGC
GAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCGGTTCTTGACAGATACTTCTATAAT
GGAGAAGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTTCGGGGCGGTGACCGAGCTG
GGGCGGCCGGACGCCAAGTACTGGAACAGCCAGAAGGAGATCCTGGAGCGGGAGCGGGCC
TATGTGGACACGTACTGCAGACACAACCTACGGGGTCGGTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTG

>ENA|JX274236|JX274236.1 Bos indicus x Bos taurus isolate Animal505 MHC
class II antigen (DRB3) gene, DRB3*1501 allele, partial cds.
CGCTCCTGTGATCAGATCTATCCTCTCTCTGCAGCACATTTCTGGAGTATTCTACGAGC

GAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCGGTACCTGGACAGATACTTCCATAAT
GGAGAAGAGTTTCGTGCGCTTCGACAGCGACTGGGGCGAGTACCGGGCGGTGACCGAGCTA
GGGCGGGCGGGTCCGCCGAGCAGTTGAACGGCCAGAAGGACACCCCTGGAGCGGGGAGCGGGCC
TATGTGGACACGTACTGCAGACACAACCTACGGGGTTCGTTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTG

>ENA|JX274237|JX274237.1 Bos indicus x Bos taurus isolate Animal506 MHC
class II antigen (DRB3) gene, DRB3*0801 allele, partial cds.
CGCTCCTGTGATCAGATCTATCCTCTCTCTGCAGCACATTTCTGGAGTATGCTACGAGC
GAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCGGTTCCTGGACAGATACTTCCATAAT
GGAGAAGAGCTCGTGCGCTTCGACAGCGACTGGGGCGAGTCCGGGCGGTGACCGAGCTG
GGGCGGGCGTCCGCCGTGCACTTGAACAGCCAGAAGGACTTCTGGAGGACGAGCGGGCT
TCGGTGGACACGTACTGCAGACACAACCTACGGGGTTCGTTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTG

>ENA|JX274238|JX274238.1 Bos indicus x Bos taurus isolate Animal507 MHC
class II antigen (DRB3) gene, DRB3*1101 allele, partial cds.
CGCTCCTGTGATCAGATCTATCCTGTCTCTGCAGCACATTTCTGCAGTATCATAAGGGC
GAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCGGTTGCTGGACAGACACTTCTATAAT
GGAGAAGAGTTCGTGCGCTTCGACAGCGACTGGGACGAGTCCGGGCGGTGACCGAGCTG
GGGCGGGCGTCCGCCGAGTACTGGAACAGCCAGAAGGACTTCTGGAGCGGAGCGGGCC
GAGGTGGACACGGTGTGCAGACACAACCTACGGGGTTCGTTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTG

>ENA|JX274239|JX274239.1 Bos indicus x Bos taurus isolate Animal520 MHC
class II antigen (DRB3) gene, DRB3*0701 allele, partial cds.
CGCTCCTGTGATCAGATCTATCCTCTCTCTGCAGCACATTTCTGGAGTATTGTAAGAGA
GAGTGTCAATTTCTTCAACGGGACCGAGCGGGTGCGGTTCTGGACAGATGCTTCCATAAT
GGAGAAGAGTTCGTGCGCTTCGACAGCGACTGGGGCGAGTCCGGGCGGTGACCGAGCTA
GGGCGGGCGGTCCGCCGAGCAGTGAACAGCCAGAAGGACTTCTGGAGGAGAGCGGGCC
GAGGTGGACAGGGTGTGCAGACACAACCTACGGGGTTCGTTGAGAGTTTCACTGTGCAGCGG
CGAGGTGAGCGCGGGGGTG

Goat

>ENA|AB008347|AB008347.1 Capra hircus DRB*01 gene for MHC class II DRB,
exon 2, partial cds.
ATCCTCTCTCTGCAGCACATTTCTGGAGTATCATAAGAGCGAGTGTCAATTTCTTCAACG
GGACCGAGCGGGTGCGGTACCTGGACAGATACTTCCATAATGGAGAAGAGTACGTGCGCT
TCGACAACGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGGCCGACGCCAAGT
ACTGGAACAGCCAGAAGGACTTCTGGAGGACAGGCGGGCCTCGGTGGACAAGTACTGCA
GATAACAACCTACGGGGTTCGGTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|AB008348|AB008348.1 Capra hircus DRB*02 gene for MHC class II DRB,
exon 2, partial cds.
ATCCTCTCTCCGCAGCACATTTCTGGAGTATCATAAGAGCGAGTGTCAATTTCTTCAACG
GGACCGAGCGGGTGCGGTACCTGGACAGATACTTCCATAATGGAGAAGAGTACGTGCGCT
TCGACAACGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGGCCGACGCCAAGT
ACTGGAACAGCCAGAAGGAGATCCTGGAGGACAGGCGGGCCTCGGTGGACAAGTACTGCA
GATAACAACCTACGGGGTTCGGTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|AB008349|AB008349.1 Capra hircus DRB*03 gene for MHC class II DRB,
exon 2, partial cds.
ATCCTCTCTCTGCAGCACATTTCTGGAGTATCATAAGAGCGAGTGTCAATTTCTTCAACG
GGACCGAGCGGGTGCGGTACCTGGACAGATACTTCCATAATGGAGAAGAGTACGTGCGCT
TCGACAACGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGGCCGACGCCAAGT
ACTGGAACAGCCAGAAGGACTTCTGGAGGACAGCCGGGCGGGCCGTGGACACGTTCTGCA
GACACAACCTACGGGGTTCATTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|AB008350|AB008350.1 Capra hircus DRB*04 gene for MHC class II DRB,
exon 2, partial cds.
ATCCTCTCTCTGCAGCACATTTCTGGAGTATTATAAGGGCGAGTGTCAATTTCTTCAACG
GGACCGAGCGGGTGCGGTTCTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCGCT
TCGACAACGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGGCAGACCGCCAAGT

ACTGGAACAGCCAGAAGGACTTCCTGGAGGACAGCCGGGCGCCGTGGACACGTTCTGCA
GACACAACACTACGGGGTCATTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|AB008351|AB008351.1 Capra hircus DRB*05 gene for MHC class II DRB,
exon 2, partial cds.

ATCCTCTCTCTGCAGCACATTTCTGGAGTATTCTACGAGCGAGTGTCATTTCTCCAACG
GGACCGAGCGGGTGCGGTTCTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCGCT
ACGACAGCGACTGGGGCGAGTACCGGGCGGTGGCCGAGCTGGGGCGGCCGAGCGCCAAGT
ACTGGAACAGCCAGAAGGAGCTCCTGGAGCAGAGGCGGACCGAGGTGGACACGTACTGCA
GACACAACACTACGGGGTCATTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|AB008352|AB008352.1 Capra hircus DRB*06 gene for MHC class II DRB,
exon 2, partial cds.

ATCCTCTCTCTGCAGCACATTTCTGGAGTATTCTACGAGCGAGTGTCATTTCTCCAACG
GGACCGAGCGGGTGCGGTTCTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCGCT
ACGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGCCGAGCGCCAAGT
ACTGGAACAGCCAGAAGGAGCTCCTGGAGCAGAGGCGGACCGAGGTGGACACGTACTGCA
GACACAACACTACGGGGTCATTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|AB008353|AB008353.1 Capra hircus DRB*07 gene for MHC class II DRB,
exon 2, partial cds.

ATCCTCTCTCTGCAGCACATTTCTGGAGTATTCTAAGAGCGAGTGTCATTTCTCCAACG
GGACCGAGCGGGTGCGGTTCTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCGCT
ACGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGCCGAACGCCAAGT
ACTGGAACAGCCAGAAGGAGATCCTGGAGGACAGGCGGGCGCCCGTGGACACGTACTGCA
GACACAACACTACGGGGTCATTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|AB008354|AB008354.1 Capra hircus DRB*08 gene for MHC class II DRB,
exon 2, partial cds.

ATCCTCTCTCTGCAGCACATTTCTGGAGTATTCTACGAGCGAGTGTCATTTCTCCAACG
GGACCGAGCGGGTGCGGTTCTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCGCT
ACGACAGCGACTGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGCCGAGCGCCAAGT
ACTGGAACAGCCAGAAGGAGATCCTGGAGGACAGCCGGGCGCCCGTGGACACGTACTGCA
GACACAACACTACGGGGTCATTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|AB008355|AB008355.1 Capra hircus DRB*09 gene for MHC class II DRB,
exon 2, partial cds.

ATCCTCTCTCTGCAGCACATTTCTGGAGTATCATAAGAGCGAGTGTCATTTCTTCAACG
GGACCGAGCGGGTGCGGTTCTGGACAGATACTTCTATAATGGAGAAGAGTACGTGCGCT
TCGACAACGACTGGGGCGAGTTCCGGGCGAGTGGCCGAGCTGGGGCGGCCGAGCGCCAAGT
ACTGGAACAGCCAGAAGGAGCTCCTGGAGCGGAGGCGGACCGAGGTGGACACGTTCTGCAGACACAACACTACGG
GGTCTTTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|AB008356|AB008356.1 Capra hircus DRB*11 gene for MHC class II DRB,
exon 2, partial cds.

ATCCTCTCTCTGCAGCACATTTCTGGAGTATACTAAGAAAGAGTGTCATTTCTCCAACG
GGACCGAGCGGGTGCGATTCTGGACAGATACTTCCATAATGGAGAAGAGTACGTGCGCT
ACGACAGCGACCGGGGCGAGTTCCGGGCGGTGGCCGAGCTGGGGCGGCCGAGGCGCGAGT
ACTGGAACAGCCAGAAGGAGATCCTGGAGCAGAAGCGGGCGGAGGCGGACACGGTGTGCA
GACACGACTACGGGGTCATTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|AB008357|AB008357.1 Capra hircus DRB*12 gene for MHC class II DRB,
exon 2, partial cds.

ATCCTCTCTCTGCAGCACATTTCTGGAGTATTCTACGAGCGAGTGTCATTTCTCCAACG
GGACCGAGCGGGTGCGGTACCTGGACAGATACTTCTATAATGGAGAAGAGAACGTGCGCT
ACGACAGCGACTGGGGCGAGTACCGGGCGGTGGCCGAGCTGGGGCGGCCGAGCGCCGAGT
ACTGGAACAGCCAGAAGGAGATTCTGGAGCGGAGGCGGACCGAGGTGGACACGGTGTGCA
GACACAACACTACGGGGTCTTTGAGAGTTTCACTGTGCAGCGGCGA

>ENA|AB008358|AB008358.1 Capra hircus DRB*13 gene for MHC class II DRB,
exon 2, partial cds.

ATCCTCTCTCTGCAGCACATTTCTGGAGTATACTAAGAAAGAGTGTCATTTCTCCAACG
GGACCGAGCGGGTGCGATTCTGGACAGATACTTCCATAATGGAGAAGAGTTCTGTGCGCT

TCGACAGCGACTGGGGCGAGTACCGGGCGGTGGCCGAGCTGGGGCGGCCGGACGCCAAGT
ACTGGAACAGCCAGAAGGAGATTCTGGAGCAGAGGCGGACCGAGGTGGACACGTA CTGCA
GACACA ACTACGGGGTCATTGAGAGTTTCACTGTGCAGCGGCCGA

>ENA|AB008360|AB008360.1 Capra hircus DRB*15 gene for MHC class II DRB,
exon 2, partial cds.

ATCCTCTCTCTGCAGCACATTTCTGGAGTATTATAAGGCCGAGTGTCATTTCTCCAACG
GGACCGGGCGGGTGCGGTTGCTGCACAGATTCTACACTAATGGAGAAGAGACCGTGCGCT
TCGACAGCGACTGGGGCGAGTTCCGGGCGGTGACCGAGCAGGGGCAGGAGGACGCCAAGT
ACTGGAACAGCCAGAAGGACTTCCTGGAGCAGAAGCGGGCCGAGGTGGACACGGTGTGCA
GACATAACTACGGGGTCCTTGAGAGTTTCACTGTGCAGCGGCCGA

>ENA|AB008361|AB008361.1 Capra hircus DRB*16 gene for MHC class II DRB,
exon 2, partial cds.

ATCCTCTCTCTGCAGCACATTTCTGGAGTATTATAAGGGCGAGTGTCATTTCTCCAACG
GGACCGGGCGGGTGCGGTTGCTGCACAGATTCTACACTAATGGAGAAGAGAACCTGCGCT
TCGACAGCGACTGGGGCGAGTTCCGGGCGGTGACCGAGCAGGGGCAGGAGGACGCCGAGT
ACTGGAACAGCCAGAAGGACTTCCTGGAGCAGAAGCGGGCCGAGGTGGACACGGTGTGCA
GACATAACTACGGGGTCCTTGAGAGTTTCACTGTGCAGCGGCCGA

>ENA|AB008362|AB008362.1 Capra hircus DRB*18 gene for MHC class II DRB,
exon 2, partial cds.

ATCCTCTCTCTGCAGCACATTTCTGAGGTATTGTAAGAGAGAGTGTCATTTCTCCAACG
GGACCGAGCGGGTGCGGCTTCTGGACAGATACTTCCATAATGGAGAAGAGATCGTGCGCT
TCGACAGCGACTGGGGCGAGTTCCGGGCGAGTGACCGAGCTGGGGCGGCCGGATGCCGAGT
ACTGGAACAGCCAGAAGGAGATCCTGGAGAGCAGGAGGACCGCGGTGGACACGTA CTGCA
GACACA ACTACGGGGTCGTTGAGAGTTTCACTGTGCAGCGGCCGA

>ENA|KM196595|KM196595.1 Capra hircus MHC class II antigen (Cahi-DRB1)
mRNA, partial cds.

TCTTCAATGGGACGGAGCAGGTGCGGTTCTGGACAGATACTACACTAATGGAGAAGAGA
CCCTGCGCTTTCGACAGCGACTGGGGCGAGTTCCGGGCGAGTGACCGAGCTGGGGCGGCCGG
ATGCCGAGTACTGGAACAGCCAGAAGGAGATCCTGGAGAGCAGGAGGACCGCGGTGGACA
CGTACTGCAGACACA ACTACG

4.2 DQA1

Sheep

>ENA|AF276954|AF276954.1 Ovis aries MHC class II antigen (DQA1) gene, DQA1-H allele, partial cds.
ACTGACTCAGCTGACCACATTGCTGCCTATGGCATAAACGTCTACCACAAATATGGTCCC
TCTGGCTACTATACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAAG
CGGGAGACTGTCTGGCATCTGCCCATGTTTGTAGTAAATTTAGACGTTTTGACCCCTCAGGGT
GCACTGAGAAACATAGCTGCAGCGAAACATAATTTGGAGGTCTTGATTCAAGATTCCAAC
TCTACTGCTGCTACCAACAATAT

>ENA|AF317617|AF317617.2 Ovis aries MHC class II antigen (OLA-DQA1) gene, OLA-DQA1*0201 allele, partial cds.
ACCTGACTCACCTGACCACATTGGCACCTATGGCGTAAACGTCTACCAAACATATGGTCC
CTCTGGCTACTATTACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAA
GAGGGAGACTGTCTGGCGTCTGCCTGTATTTAGTAAATTTGCAAGTTTTGACCCCTCAGGG
TGCACTGAGAAACATAGCTGTGGGGAAACAGTCTTTGGAGATCTTGATTCAAAGGTCCAA
CTCTACTGCTGCTACCAACAGTATGTGTT

>ENA|AY229894|AY229894.1 Ovis aries MHC class II antigen (DQA1) gene, OLA-DQA1*0801 allele, exon 2 and partial cds.
ACCTGACTCACCTGACCACATTGCCGCCTATGGCGTAAACGTCTACCAAACATATGGTCC
CTCTGGCTACTATACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAA
GAAGGAGACTGTCTGGCATCTGCCTGTGTTTGTAGTCAATTTAGAAGTTTTGACCCCTCAGGG
TGCACTGAGAAACATAGCTACAGCGAAACATAATTTGGAGATCACGATTCAAAGGTCCAA
CTCTACTGCTGCTACCAACAGTATGTGTT

>ENA|AY265308|AY265308.1 Ovis aries MHC class II antigen (OLA-DQA1) gene, OLA-DQA1*0401 allele, exon 2 and partial cds.
ACCTGACTCACCTGACCACATTGGCACCTATGGCGTAAACGTCTACCAAACATATGGTTC
TTCTGGCTACTATACCCATGAATTTGATGGAGATGAACAATTCTACGTGGACCTGGAAAA
GCGGGAGACTGTCTGGCGTCTACCTATGTTTGTAGTAAATTTACAAGTTTGTGACGCTCAGTT
TGCACTGAGAAACATAGCTACGTTCAAACATAATTTGGAGCTCATGATTCAGAGGTCCAA
CTCTACTGCTGCTACCAACAGTATGTGTT

>ENA|AY230209|AY230209.1 Ovis aries MHC class II antigen (OLA-DQA1) gene, OLA-DQA1*0104 allele, exon 2 and partial cds.
ACCTGACTCACCTGACCACATTGGCACCTATGGCGTAAACATCTACCAAACATATGGTCC
CTCTGGCTACTATACCCATGAATTTGATGGAGATGAAGAGTTCCACGTGGACCTGGAAAA
GAGGGAGACTGTCTGGCGTCTGCCTGAGTTTGTAGTAAATTTACAAGTTTGTGACCCCTCAGGG
TGCACTGAGAAACATAGCTACGGTGAAACATAATTTGGAGATCTTGATTCAAAGGTCCAA
CTCTACTGCTGCTACCAACAGTATGTGTT

>ENA|AY230210|AY230210.1 Ovis aries MHC class II antigen (OLA-DQA1) gene, OLA-DQA1*0102 allele, exon 2 and partial cds.
ACCTGACTCACCTGACCACATTGGCATCTATGGCGTAAACGTCTACCAAACATATGGTCC
CTCTGGCTACTATACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAA
GAGGGAGACTGTCTGGCGTCTGCCTGAGTTTGTAGTAAATTTACAAGTTTGTGACCCCTCAGGG
TGCACTGAGAAACATAGCTACGACGAAACATAATTTGGAGATCTTGATTCAAATGTCCAA
CTCTACTGCTGCTACCAACAGTATGTGTT

>ENA|Z28420|Z28420.1 O.aries (cosmid4) MHC class II DQA1 gene, exon 2
CAGCTGACCACATTGCCGCCTATGGCATAAATGTCTACCACTCATATGGTCCCTCTGGCT
ACTATACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAAGAGGGAGA
CTGTCTGGCGTCTGCCTGTGTTTGTAGTCAATTTAGAAGGTTTGATCCTCAGGGTGCACTGA

GAAACATCGCTGTGGGGAAACAGTCTTTGGAGATCTTGATTCAAAGGTCCAACTCTACTG
CTGCTACCAACAGTAAGTGTTCGCCATTCTGCCTCTCTTTATTAATCTACCCCTTCATGC
CAGCGTTCACTCCCTTTTTCTCTAGGGATAGATACCCTTCACCGCTTTATAAACTCTCTC CTTTCCAAGGAC

Cattle

>ENA|AB257101|AB257101.1 Bos taurus BoLA-DQA1 gene for MHC class II antigen, partial cds, allele: BoLA-DQA1*1203.
AATTTCTTCTTTCACTTTGCTTAATAAGGGTCTTTTCTCTATTTTTCCCTTTCTTGCTCC
TCACTCCGACTCAGCTGACCACATTGGCACCTATGGCATAAGCATCTACCACACATATGG
TCCCTCTGGCTACTATACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGA
AAAGAGGGGAGACTGTCTGGCGTCTGCCTGTGTTTAGTAAATTTGCAACTTTTGACCCCTCA
GGGTGCGCTGAGAAACATAGCTACGTGCAAGCACGATTTGGAGGTCTTGATTCAAAGGTC
CAACTCTACTGCTGCT

>ENA|AB257102|AB257102.1 Bos taurus BoLA-DQA1 gene for MHC class II antigen, partial cds, allele: BoLA-DQA1*0801.
AATTTCTTCTTTCACTTTGCTTAATAAGGGTCTTTTCTCTATTTTTCCCTTTCTTGCTCC
TCACTCCGACTCAGCTGACCACATTGGCGCCTATGGCATAAACGTCTACCACATATGG
TCCCTCTGGCTACTATACCCATGAATTTGATGGAGATGAACAGTTCTACGTGGACCTGGA
AAAGAGGGGAGACTGTCTGGCGTCTGCCTGTGTTTAGTAAATTTGCAAGTTTTGACCCCTCA
GGGTGCGCTGAGAAACATAGCTACAGCGAAGCACAAATTTGGAGATTATGATTCAAAGAGTC
CAACTCTACTGCTGCT

>ENA|AB257103|AB257103.1 Bos taurus BoLA-DQA1 gene for MHC class II antigen, partial cds, allele: BoLA-DQA1*0101.
AATTTCTTCTTTCACTTTGCTTAATAAGGGTCTTTTCTCTATTTTTCCCTTTCTTGCTCC
TCACTCCGACTCAGCTGACCACATTGGCGCCTATGGCATAAACGTCTACCACACATATGG
TCCCTCTGGCTACTATACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGA
AAAGAGGGGAGACTGTCTGGCGTCTGCCTGTGTTTAGTAAATTTACAAGTTTTGACCCCTCA
GGGTGCGCTGAGAAACATAGCTACAGCGAAGCACAAATTTGGAGGTCTTGATTCAAAGGTC
CAACTCTACTGCTGCT

>ENA|AB257104|AB257104.1 Bos taurus BoLA-DQA1 gene for MHC class II antigen, partial cds, allele: BoLA-DQA1*0203-1.
AATTTCTTCTTTCACTTTGATTAATAAGGGTCTTTTCTCTATTTTTCCCTTTCTTGCTCC
TCACTCCGACTCAGCTGACCACATTGGCGCCTATGGCATAAACGTCTACCACACATATGG
TCCCTCTGGCTACTATACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGA
AAAGAGGGGAGACTGTCTGGAATCTGCCTCTGTTTAGTAAATTTAGACGTTTTGACCCCTCA
GGGTGCGCTGAGAAACATAGCTACAGTGAAGCACAAATTTGGAGATCGTGATTCAAAGGTC
CAACTCTACTGCTGCT

>ENA|AB257105|AB257105.1 Bos taurus BoLA-DQA1 gene for MHC class II antigen, partial cds, allele: BoLA-DQA1*0204.
AATTTCTTCTTTCACTTTGCTTAATAAGGGTCTTTTCTCTATTTTTCCCTTTCTTGCTCC
TCACTCCGACTCAGCTGACCACATTGGTGCCTATGGCATAAACATCTACCACACATATGG
TCCCTCTGGCTACTATACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGA
AAAGAGGGGAGACTGTCTGGAATCTGCCTCTGTTTAGTAAATTTAGACGTTTTGACCCCTCA
GGGTGCGCTGAGAAACATAGCTACAGCGAAGCACAAATTTGGAGATCGTGATTCAAAGGTC
CAACTCTACTGCTGCT

>ENA|AB257106|AB257106.1 Bos taurus BoLA-DQA1 gene for MHC class II antigen, partial cds, allele: BoLA-DQA1*0301.
AATTTCTTCTTTCACTTTGCTTAATAAGGGTCTTTTCTCTATTTTTCCCTTTCTTGCTCC
TCACTCCGACTCAGCTGACCACATTGGCGCCTATGGCATAAACGTCTACCACATATGG
TCCCTCTGGCTACTATACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGA
AAAGAGGGGAGACTGTCTGGAATCTGCCTCTGTTTAGTAAATTTAGACGTTTTGACCCCTCA
GGGTGCGCTGAGAAACATAGCTACGACGAAGCACAAATTTGGAGATCATGATGCAAAGGTC
CAACTCTACTGCTGCT

>ENA|AB257107|AB257107.1 Bos taurus BoLA-DQA1 gene for MHC class II antigen, partial cds, allele: BoLA-DQA1*0401.

AATTTCTTCTTTCACTTTGATTAATAAGGGTCTTTTCTCTATTTTCCCTTTCTTGCTCC
TCACTCCGACTCAGCTGACCACATTGGCGCCTATGGCATAAACGTCTACCACTCATATGG
TCCCTCTGGCTACTATAACCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGA
AAAGAGGGGAGACTGTCTGGAATCTGCCTCTGTGTTAGTAAATTTAGACGTTTTGACCTCA
GGGTGCGCTGAGAAACATAGCTACAGCGAAGCACAATTTGGAGGTCTTGATTCAAAGGTC
CAACTCTACTACTGCT

>ENA|AB257108|AB257108.1 Bos taurus BoLA-DQA1 gene for MHC class II
antigen, partial cds, allele: BoLA-DQA1*0103.

AATTTCTTCTTTCACTTTGCTTAATAAGGGTCTTTTCTCTATTTTCCCTTTCTTGCTCC
TCACTCCGACTCAGCTGACCACATTGGTGCCTATGGCATAAACGTCTACCACACATATGG
TCCCTCTGGCTACTATAACCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGA
AAAGAGGGGAGACTGTCTGGCGTCTGCCTGTGTGTTAGTAAATTTACAAGTTTTGACCTCA
GGGTGCGCTGAGAAACATAGCTACGACGAAGCACAATTTGGAGATCATGATTCAAAGGTC
CAACTCTACTGCTGCT

>ENA|AB257109|AB257109.1 Bos taurus BoLA-DQA1 gene for MHC class II
antigen, partial cds, allele: BoLA-DQA1*10011.

AATTTCTTCTTTCACTTTGCTTAATAAGGATCTTTTCTCTATTTTCCCTTTCTTGCTCC
TCACTCCGACTCAGCTGACCACATTGGCACCTATGGCATAAGCATCTACCACACATATGG
TCCCTCTGGCTACTATAACCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTAGA
AAAGAGGGGAGACTGTCTGGCGTCTGCCTGTGTGTTAGTAAATTTACAAGTTTTGACCTCA
GGGTGCGCTGAGAAACATAGCTATAGTGAAGCACAATTTGGAGATCGTGATTCAAAGGTC
CAACTCTACTGCTGCT

>ENA|AB257110|AB257110.1 Bos taurus BoLA-DQA1 gene for MHC class II
antigen, partial cds, allele: BoLA-DQA1*12011.

AATTTCTTCTTTCACTTTGCTTAATAAGGGTCTTTTCTCTATTTTCCCTTTCTTGCTCC
TCACTCCGACTCAGCTGACCACATTGGCACCTATGGCATAAGCATCTACCACACATATGG
TCCCTCTGGCTACTATAACCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGA
AAAGAGGGGAGACTGTCTGGCGTCTGCCTGTGTGTTAGTAAATTTGCAACTTTTGACCTCA
GGGTGCGCTGAGAAACATAGCTACGACGAAGCACAATCTGGAGATCGTGATTCAAAGGTC
CAACTCTACTGCTGCT

>ENA|AB257111|AB257111.1 Bos taurus BoLA-DQA1 gene for MHC class II
antigen, partial cds, allele: BoLA-DQA1*12012.

AATTTCTTCTTTCACTTTGCTTAATAAGGGTCTTTTCTCTATTTTCCCTTTCTTGCTCC
TCACTCCGACTCAGCTGACCACATTGGCACCTATGGCATAAGCATCTACCACACATATGG
TCCCTCTGGCTACTATAACCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGA
AAAGAGGGGAGACTGTCTGGCGTCTGCCTGTGTGTTAGTAAATTTGCAACTTTTGACCTCA
GGGTGCGCTGAGAAACATAGCTACGACGAAGCACAATTTGGAGATCGTGATTCAAAGGTC
CAACTCTACTGCTGCT

>ENA|AB257112|AB257112.1 Bos taurus BoLA-DQA1 gene for MHC class II
antigen, partial cds, allele: BoLA-DQA1*1401.

AATTTCTTCTTTCACTTTGCTTAATAAGGGTCTTTTCTCTATTTTCCCTTTCTTGCTCC
TCACTCCGACTCAGCTGACCACATTGGCGCCTATGGCATAAACGTCTACCACTCATATGG
TCCCTCTGGCTACTATAACCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGA
AAAGAGGGGAGACTGTCTGGCGTCTGCCTGTGTGTTAGTAAATTTGCAAGTTTTGACCTCA
GGGTGCGCTGAGAAACATAGCTGTGGGGAAACGGACTTTGGAGGTCTGATTCAAAGGTC
CAACTCTACTGCTGCT

>ENA|AB257113|AB257113.1 Bos taurus BoLA-DQA1 gene for MHC class II
antigen, partial cds, allele: BoLA-DQA1*12021.

AATTTCTTCTTTCACTTTGCTTAATAAGGGTCTTTTCTCTATTTTCCCTTTCTTGCTCC
TCACTCCGACTCAGCTGACCACATTGGCACCTATGGCATAAGCATCTACCACACATATGG
TCCCTCTGGCTACTATAACCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGA
AAAGAGGGGAGACTGTCTGGCGTCTGCCTGTGTGTTAGTAAATTTGCAACTTTTGACCTCA
GGGTGCGCTGAGAAACATAGCTACGATGAAGCACAATTTGGAGATCGTGATTCAAAGGTC
CAACTCTACTGCTGCT

>ENA|AB259566|AB259566.1 Bos taurus BoLA-DQA1 gene for MHC class II antigen, partial cds, allele: BoLA-DQA1*10012.
AATTTCTTCTTTTCACTTTTGCTTAATAAGGATCTTTTCTCTATTTTCCCTTTCTTGCTCC
TCACTCGGACTCAGCTGACCACATTGGCAGCTATGGCATAAGCATCTACCACACATATGG
TCCCTCTGGCTACTATACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGA
AAAGAGGGGAGACTGTCTGGCGTCTGCCTGTGTTTAGTAAATTTACAAGTTTTGACCCCTCA
GGGTGCGCTGAGAAACATAGCTATAGTGAAGCACAATTTGGAGATCGTGATTCAAAGGTC
CAACTCTACTGCTGCT

>ENA|AB259567|AB259567.1 Bos taurus BoLA-DQA1 gene for MHC class II antigen, partial cds, allele: BoLA-DQA1*0102.
AATTTCTTCTTTTCACTTTTGCTTAATAAGGGTCTTTTCTCTATTTTCCCTTTCTTGCTCC
TCACTCCGACTCAGCTGACCACATTGGCGCCTATGGCATAAACGTCTACCACACATATGG
TCCCTCTGGCTACTATACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGA
AAAGAGGGGAGACTGTCTGGCGTCTGCCTGTGTTTAGTAAATTTACAAGTTTTGACCCCTCA
GGGTGCGCTGAGAAACATAGCTACAGTGAAGCACAATTTGGAGATCTTGATTCAAAGGTC
CAACTCTACTGCTGCT

>ENA|KC820982|KC820982.1 Bos taurus MHC class II antigen (BoLA-DQA) gene, BoLA-DQA*0106 allele, exon 2 and partial cds.
TCAATTTCTTCTTTTCACTTTTGCTTAATAAGGGTCTTTTCTCTATTTTCCCTTTCTTGCT
CCTCACTCCGACTCAGCTGACCACATTGGCGCCTATGGCATAAACGTCTACCACACATAT
GGTCCCTCTGGCCACTATACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTG
GAAAAGAGGGGAGACTGTCTGGCGTCTGCCTGTGTTTAGTAAATTTACAAGTTTTGACCCCT
CAGGGTGCGCTGAAAAACATAGCTACAGCGAAGCACAATTTGGAGGTCTTGCTTCAAAGG
TCCAACCTCTCTGCTGCTACCAACAGTATGTGTCCCCACTCTGCCTCTCTTTATTAATCT
ACCCCTTCAAACC

>ENA|KC820983|KC820983.1 Bos taurus MHC class II antigen (BoLA-DQA) gene, BoLA-DQA*3301 allele, exon 2 and partial cds.
TCAATTTCTTCTTTTCACTTTTGCTTAATAAGGGTCTTTTCTCTATTTTCCCTTTCTTGCT
CCTCACTCCGACTCAGCTGACCACATTGGCGCCTATGGCATAAACGTCTACCACACATAT
GGTCCCTCTGGCTACTATACCCAAGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTG
GAAAAGAGGGGAGGCTGTCTGGCGTCTGCCTGTGTTTAGTAAATTTACAAGTTTTGACCCCT
CAGGGTGCGCTGAGAAACCCAGCTTCAGCGAAGCACAATTTGGAGGTCTTGATTCAAAGG
TCCAACCTCTCTGCTGCTACCAACAGTATGTGTCCCCACTCTGCCTCTCTTTATTAATCT
ACCCCTTCAAACC

>ENA|U80869|U80869.1 Bos taurus MHC class II antigen (BoLA-DQA1) gene, allele 1b, partial cds.
GACCACATTGGCGCCTATGGCATAAACGTCTACCACTCATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGGAGACTGTC
TGGCGTCTGCCTGTGTTTAGTAAATTTGCAAGTTTTGACCCCTCAGGGTGCGCTGAGAAAC
ATAGCTGTGGGGAAACGGACTTTGGAGGTCATGATTGCAAGGTCCAACCTCTACTGCTGCT ACCAAC

>ENA|U80870|U80870.1 Bos taurus MHC class II antigen (BoLA-DQA1) gene, allele 3b, partial cds.
GACCACATTGGCGCCTATGGCATAAACGTCTACCACTCATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGGAGACTGTC
TGGAATCTGCCTCTGTTTAGTAAATTTAGACGTTTTGACCCCTCAGGGTGCGCTGAGAAAC
ATAGCTACGACGAAGCACAATTTGGAGATCATGATGCAAAGGTCCAACCTCTACTGCTGCT ACCAAC

>ENA|U80871|U80871.1 Bos taurus MHC class II antigen (BoLA-DQA1) gene, allele 3c, partial cds.
GACCACATTGGCGCCTATGGCATAAACGTCTACCACTCATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGGAGACTGTC
TGGAATCTGCCTCTGTTTAGTAAATTTAGACGTTTTGACCCCTCAGGGTGCGCTGAGAAAC
ATAGCTACAGCGAAGCACAATTTGGAGGTCTTGATTCAAAGGTCCAACCTCTACTACTGCT ACCAAC

>ENA|U80872|U80872.1 Bos taurus MHC class II antigen (BoLA-DQA1) gene, allele 3a, partial cds.
GACCACATTGGTGCCTATGGCATAAACATCTACCACACATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGGAGACTGTC

TGGAATCTGCCTCTGTTTAGTAAATTTAGACGTTTTGACCCTCAGGGTGCGCTGAGAAAC
ATAGCTACAGCGAAGCACAATTTGGAGATCGTGATTCAAAGGTCCAACCTCTACTGCTGCT ACCAAC

>ENA|U80873|U80873.1 Bos taurus MHC class II antigen (BoLA-DQA1) gene,
allele 2, partial cds.

GACCACATTGGCGCCTATGGCATAAACGTCTACCACACATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTC
TGGAATCTGCCTCTGTTTAGTAAATTTAGACGTTTTGACCCTCAGGGTGCGCTGAGAAAC
ATAGCTACAGTGAAGCACAATTTGGAGATCGTGATTCAAAGGTCCAACCTCTACTGCTGCT ACCAAC

>ENA|U80874|U80874.1 Bos taurus MHC class II antigen (BoLA-DQA1) gene,
allele 8, partial cds.

GACCACATTGGCGCCTATGGCATAAACGTCTACCACTCATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAACAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTC
TGGCGTCTGCCTGTGTTTAGTAAATTTGCAAGTTTTGACCCTCAGGGTGCGCTGAGAAAC
ATAGCTACAGCGAAGCACAATTTGGAGATTATGATTCAAAGAGTCCAACCTCTACTGCTGCT ACCAAC

>ENA|U80875|U80875.1 Bos taurus MHC class II antigen (BoLA-DQA1) gene,
allele 7c, partial cds.

GACCACATTGGCGCCTATGGCATAAACGTCTACCACTCATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAACAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTC
TGGCGTCTGCCTGTGTTTAGTAAATTTGCAAGTTTTGACCCTCAGGGTGCGCTGAGAAAC
ATAGCTACAGCGAAGCACAATTTGGAGATTATGATTCAAAGAGTCCAACCTCTACTGCTTCT ACCAAC

>ENA|U80876|U80876.1 Bos taurus MHC class II antigen (BoLA-DQA1) gene,
allele 9a, partial cds.

GACCACATTGGCACCTATGGCATAAGCATCTACCACACATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTC
TGGCGTCTGCCTGTGTTTAGTAAATTTGCAACTTTTGACCCTCAGGGTGCGCTGAGAAAC
ATAGCTACGTGCAAGCACGATTTGGAGGTCTTGATTCAAAGGTCCAACCTCTACTGCTGCT ACCAAC

>ENA|U80877|U80877.1 bos taurus Bovine MHC class II antigen (BoLA-DQA1)
gene, allele 12, partial cds.

GACCACATTGGCACCTATGGCATAAGCATCTACCACACATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTC
TGGCGTCTGCCTGTGTTTAGTAAATTTGCAACTTTTGACCCTCAGGGTGCGCTGAGAAAC
ATAGCTACGACGAAGCACAATCTGGAGATCGTGATTCAAAGGTCCAACCTCTACTGCTGCT ACCAAC

>ENA|U80878|U80878.1 Bos taurus MHC class II antigen (BoLA-DQA1) gene,
allele 11a, partial cds.

GACCACATTGGCACCTATGGCATAAGCATCTACCACACATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTC
TGGCGTCTGCCTGTGTTTAGTAAATTTGCAACTTTTGACCCTCAGGGTGCGCTGAGAAAC
ATAGCTACGATGAAGCACAATTTGGAGATCGTGATTCAAAGGTCCAACCTCTACAGCTGCT ACCAAC

>ENA|U80879|U80879.1 Bos taurus MHC class II antigen (BoLA-DQA1) gene,
allele 11d, partial cds.

GACCACATTGGCGCCTATGGCATAAACGTCTACCACACATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTC
TGGCGTCTGCCTGTGTTTAGTAAATTTGCAACTTTTGACCCTCAGGGTGCGCTGAGAAAC
ATAGCTACGATGAAGCACAATTTGGAGATCGTGATTCAAAGGTCCAACCTCTACTGCTGCT ACCAAC

>ENA|U80880|U80880.1 Bos taurus MHC class II antigen (BoLA-DQA1) gene,
allele 11b, partial cds.

GACCACATTGGCACCTATGGCATAAGCATCTACCACACATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTAGAAAAGAGGGAGACTGTC
TGGCGTCTGCCTGTGTTTAGTAAATTTACAAGTTTTGACCCTCAGGGTGCGCTGAGAAAC
ATAGCTATAGTGAAGCACAATTTGGAGATCGTGATTCAAAGGTCCAACCTCTACTGCTGCT ACCAAC

>ENA|U80881|U80881.1 Bos taurus MHC class II antigen (BoLA-DQA1) gene,
allele 10, partial cds.

GACCACATTGGCACCTATGGCATAAGCATCTACCACACATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTC

TGGCGTCTGCCTGTGTTTAGTAAATTTACAAGTTTTGACCCTCAGGGTGCGCTGAGAAAC
ATAGCTATAGTGAAGCACAATTTGGAGATCGTGATTCAAAGGTCCAACCTCTACTGCTGCT ACCAAC

>ENA|U80882|U80882.1 Bos taurus MHC class II antigen (BoLA-DQA1) gene,
allele 1d, partial cds.

GACCACATTGGTGCCTATGGCATAAACGTCTACCACACATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTC
TGGCGTCTGCCTGTGTTTAGTAAATTTACAAGTTTTGACCCTCAGGGTGCGCTGAGAAAC
ATAGCTACGACGAAGCACAATTTGGAGATCATGATTCTGAAGGTCCAACCTCTACTGCTGCT ACCAAC

>ENA|U80883|U80883.1 Bos taurus MHC class II antigen (BoLA-DQA1) gene,
allele 1a, partial cds.

GACCACATTGGCGCCTATGGCATAAACGTCTACCACACATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTC
TGGCGTCTGCCTGTGTTTAGTAAATTTACAAGTTTTGACCCTCAGGGTGCGCTGAGAAAC
ATAGCTACAGCGAAGCACAATTTGGAGGTCTTGATTCAAAGGTCCAACCTCTACTGCTGCT ACCAAC

>ENA|U80884|U80884.1 Bos taurus MHC class II antigen (BoLA-DQA1) gene,
allele 4a, partial cds.

GACCACATTGGCGCCTATGGCATAAACGTCTACCACACATATGGTCCCTCTGGCTACTAT
ACCCATGAATTTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTC
TGGCGTCTGCCTGTGTTTAGTAAATTTACAAGTTTTGACCCTCAGGGTGCGCTGAGAAAC
ATAGCTACAGTGAAGCACAATTTGGAGATCTTGATTCAAAGGTCCAACCTCTACTGCTGCT ACCAAC

>ENA|Z79507|Z79507.1 B.primigenius BoLADQA1 gene (isolate 3)

GCCTATGGCATAAACGTCTACCACACATATGGTCCCTCTGGCTACTATACCCATGAATTT
GATGGAGATGAACAGTTCTACGTGGACCTGGAAAAGAAGGAGACTGTCTGGCGTCTGCCT
GTGTTTAGTAAATTTGCAACTTTTGACCCTCAGGGTGCGCTGAGAAACATAGCTGTGGGG
AAACAGACTTTGGAGGTCATGATTCTGAAGGTCCAACCTCTAC

>ENA|Z79514|Z79514.1 B.primigenius BoLADQA1 gene (isolate 14)

TCCTATGGCACAGAGATCTACCAATCTCATGGTCCCTCTGGCCAGTACACCCAGGAATTT
GATGGAGACGAGCTGTTTTATGTGGACCTGGGGAAGAAGGAGACTGTCTGGAGGCTGCCT
ATGTTTAGCCAGTTTGCAGGGTTTGACCCACAGGCTGCACTGAGTGAAATAGCTACAGCA
AAACACAACCTTGGATGTCCTGACTAAACGCTCCAACCTTTAC

>ENA|Z79515|Z79515.1 B.primigenius BoLADQA1 gene (isolate E55)

TCCTATGGCACAGAGATCTACCAATCTCATGGTCCCTCTGGCCAGTACACCCAGGAATTT
GATGGAGACGAGATGTTTTATGTGGACCTGGGGAAGAAGGAGACTGTCTGGAGGCTGCCT
AGTTTTAGCCAGTTTGCAGGTTTTGACCCACAAGCTGCACTGAGTGAAATAGCTACATCA
AAACACAACCTTGGATGTCCTGACTAAACGCTCCAACCTTTAC

>ENA|Z79516|Z79516.1 B.primigenius BoLADQA1 gene (isolate F187)

TCCTACGGCACAGAGATCTACCAATCTCATGGTCCCTCTGGCCAGTACACCCAGGAATTT
GATGGAGACGAGATGTTTTATGTGGACCTGGGGAAGAAGGAGACTGTCTGGAGGCTGCCT
ATGTTTAGCCAGTTTGCAGGTTTTGCCCCACAGGCTGCACTGAGTGAAATAGCTACATCA
AAACACAACCTTGGATGTCCTGACTAAACGCTCCAACCTTTAC

>ENA|Z79517|Z79517.1 B.primigenius BoLADQA1 gene (isolate NKB1)

TCCTATGGCACAGAGATCTACCAATCTCATGGTCCCTCTGGCCAGTACACCCAGGAATTT
GATGGAGACGAGCTGTTTTATGTGGACCTGGGGAAGAAAGAGACTGTCTGGAGGCTGCCT
ATGTTTAGCCAGTTTGCAGGGTTTGACCCACAGGCTGCACTGAGTGAAATAGCTACAGCA
AAACACAACCTTGGATGTCCTGACTAAACGCTCCAACCTTTAC

>ENA|Z79518|Z79518.1 B.primigenius BoLADQA1 gene (isolate NK10)

TCCTATGGCACAGAGATCTACCAATCTCATGGTCCCTCTGGCCAGTACACCCAGGAATTT
GATGGAGACGAGATGTTTTATGTGGACCTGGGGAAGAAAGAGACTGTCTGGAGACTGCCT
ATGTTTAGCCAGTTTGCAGGGTTTGACCCACAGGCTGCACTGAGTGAAATAGCTACAGCA
AAACACAACCTTGGATGTCCTGACTAAACGCTCCAACCTTTAC

>ENA|Z79519|Z79519.1 B.primigenius BoLADQA1 gene (isolate 12)

ACTTATGGCACAGACTTCTACCAATCTCATGGTCCCTCTGGCCAGTACATCCACCAATTT
GATGGAGACGAGGAGTTTTATGTGGACCTGGAGAAGGAAGAGGCTGTCTGGAGGCTGCCT

ATGTTTGATAAATTAAGACGTTTTTCACCCGCAAGGTGCACTGAGAGACATAGCTGTAGCG
AAACACAACCTTGGATGTCCTGACTAAACGCTACAACCTTTAC

>ENA|Z79520|Z79520.1 B.primigenius BoLADQA1 gene (isolate 12)
ACCTACGGTGCAGACTTCTACCAATCTCATGGTCCCTCTGGCCAGTACATCCATGAATTT
GATGGAGATGAGTTGTTTTATGTGGACCTGGGGAAGAAGGAGACTGTCTGGCAGCTGCCT
ATGTTTGGTGAATTAACAAGTTTTGAAGCACAAGATGCGCTGAATGAAATAGCTAAAGCA
AAACACACCTTGGATGTCCTGACTAAACGCTCCAACCTTTAC

>ENA|Z79521|Z79521.1 B.primigenius BoLADQA1 gene (isolate 14)
ACTTATGGCACAGACTTCTACCAATCTCATGGTCCCTCTGGCCAGTACATCCACCAATTT
GATGGAGACGAGGAGTTTTATGTGGACCTGGAGAAGGAAGAGGCTGTCTGGAGGCTGCCT
ATGTTTGATAAATTAAGACGTTTTTCACCCGCAAGGTGCACTGAGAACATAGCTATAGCGAAA
CACAACCTTGGATGTTCTGACAAAACCTCTACAACCTTTACCCC

>ENA|Z79522|Z79522.1 B.primigenius BoLADQA1 gene (isolate 19)
TCCTATGGCATAGACTTCTACCAATCTCATGGTCCCTCTGGCCAGTACATCCATGAATTT
GATGGAGACGAGATGTTTTATGTGGATCTGGGGAAGAAGGAGACTGTCTGGAGGCTGCCT
ATGTTTGGTGAATTAACAGGTTTTGACCCGCAAGGTGCACTGAGGAACATAGCTACAGAA
AAACACAACCTTGGATATCTTGACTAAATGCTCCAACCTTTAC

>ENA|Z79523|Z79523.1 B.primigenius BoLADQA1 gene (isolate E223)
ACTTATGGCACAGACTTCTACCAATCTCATGGTCCCTCTGGCCAGTACATCCACCAATTT
GATGGAGACGAGGAGTTTTATGTGGACCTGGAGAAGGAAGAGGCTGTCTGGAGGCTGCCT
ATGTTTGATAAATTAAGACGTTTTTCACCCGCAAGGTGCACTGAGAAAACATAGCTGTAGCG
AAACACAACCTTGGATGTCCTGACTAAACGCTACAACCTTTAC

>ENA|Z79524|Z79524.1 B.primigenius BoLADQA1 gene (isolate E55)
ACCTACGGCGCAGACTTCTACCAATCTCATGGTCCCTCTGGCCAGTACATCCACGAATTT
GATGGAGACGAGTTGTTTTATGTGGACCTGGGGAAGAAGGAGACTGTCTGGCAGCTGCCT
ATGTTTGGTGAATTAACAAGTTTTGAAGCACAAGATGCGCTGAATGAAATAGCTAAAGCA
AAACACACCTTGGATGTCCTGACTAAACGCTCCAACCTTTAC

>ENA|Z79525|Z79525.1 B.primigenius BoLADQA1 gene (isolate G123)
ACCTACGGCGCAGAAATCTACCAATCTCATGGTCCCTCTGGCCAGTACATCCACGAATTT
GATGGAGATGAGTTGTTTTATGTGGACCTGGGGAAGAAGGAGACTGTCTGGCAGCTGCCT
ATGTTTGGTGAATTAACAAGTTTTGAAGCACAAGATGCGCTGATGAAATAGCTAAAGCAA
AACACACCTTGGATGTCCTGACTAAACGCTCCAACCTTTACC

>ENA|Z79526|Z79526.1 B.primigenius BoLADQA1 gene (isolate G307)
ACTTATGGCACAGACTTCTACCAATCTCATGGTCCCTCTGGCCAGTACATCCACCAATTT
GATGGAGACGAGGAGTTTTATGTGGACCTGGAGAAGGAAGAGGCTGTCTGGAGGCTGCCT
ATGTTTGATAAATTAAGACGTTTTTCACCCGCAAGGTGCACTGAGAAAACATAGCTATAGCG
AAACACAACCTTGGATGTTCTGACAAAACCTCTACAACCTTTAC

Goat

>ENA|AY464656|AY464656.1 Capra hircus major histocompatibility class II
DQA1 (Cahi-DQA1) gene, Cahi-DQA1.4 allele, exon 2 and partial cds.
AAGCCCACAATGTTTGATAGTCAATTTCTTCTTCACTTGCTTAATGAGGATCTTTTCTC
TATTTTTCCTTTCTTGCTCCTCAGCTACCCGACTCAGCTGACCACATTGGCATCTATGGCGT
AAACGCTTACCAACATATGGTCCCTCTGGCTACTTTACCCATGAATTTGATGGAGATGA
AGAGTTCTACGTGGACCTGGAAAAGAAGGAGACTGTCTGGCATCTGCCTGTGTTTAGTCA
ATTTAGAAGGTTTGACCCTCAGGGTGCAGTGAAGAACATAGCTGCAGCGAAACATAATTT
GGAGATCACGATTCAAAGGTCCAACCTCTACTGCTGCTACCAACAGTATGTGTTTACCATT
CTGCCTCTCTTTGTTGTTCTTCCCC

>ENA|AY464657|AY464657.1 Capra hircus major histocompatibility class II
DQA1 (Cahi-DQA1) gene, Cahi-DQA1.1 allele, exon 2 and partial cds.
AAGCCCACAATGTTTGATAGTCAATTTCTTCTTCACTTGCTTAATGAAGATCTTTTCTCT
ATTTTTTCCTTTCTTGCTCCTCACCCTGACTCAGCTGACCACATTGGCATCTATGGCGTA
AACGCTTACCAACATATGGTCCCTCTGGCTACTATACCCATGAATTTGATGGAGATGAA

GAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTCTGGCGTCTGCCTGAGTTTAGTAAA
 TTTACAAGTTTTGACCCTCAGGGTGCAGTCTGAGAAACATAGCTACGGCGAAACATAATTTG
 GAGATCTTGATTCAAAGGTCCAACCTCTACTGCTGCTACCAACAGTATGTGTTTACCATTCT
 TGCCTCTCTTTGTTGTTCTTCCCC

>ENA|AY665664|AY665664.1 Capra hircus MHC class II antigen (Cahi-DQA1)
 gene, Cahi-DQA1.5 allele, partial cds.

AAGCCCACAATGTTTGATAGTCAATTTCTTCTTTCACTGCTTAATGAAGATCTTTTCTCT
 ATTTTTCCCTTTCTGGCTCCTCACCTGACTCAGCTGACCACATTGGCACCTATGGCATA
 AGCATCTACCAAACATATGGTCCCTCTGGCTACTATACCCATGAATTTGATGGAGATGAA
 GAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTCTGGCGTCTGCCTGAGTTTAGTAAA
 TTTGCAAGTTTTGACCCTCAGGGTGCAGTCTGAGAAACATAGCCACGATAAAACATAATTTG
 GAGGTCTTGATTCAAAGGTCCAACCTCTACTGCTGCTACCAACAGTATGTGTTTACCATTCT
 TGCCTCTCTTTGTTGTTCTTCCCC

>ENA|AY665665|AY665665.1 Capra hircus MHC class II antigen (Cahi-DQA1)
 gene, Cahi-DQA1.7 allele, partial cds.

AAGCCCACAATGTTTGATAGTCAATTTCTTCTTTCACTGCTTAATGAAGATCTTTTCTCT
 ATTTTTCCCTTTCTGGCTCCTCACCTGACTCAGCTGACCACATTGGCATCTATGGCGTA
 AACGTCTACCAAACATATGGTCCCTCTGGCTACTTTACCCATGAATTTGATGGAGATGAA
 GAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTCTGGCGTCTGCCTGAGTTTAGTAAA
 TTTACAAGTTTTGACCCTCAGGGTGCAGTCTGAGAAACATAGCTACGGCGAAACATAATTTG
 GAGATCTTGATTCAAAGGTCCAACCTCTACTGCTGCTACCAACAGTATGTGTTTACCATTCT
 TGCCTCTCTTTGTTGTTCTTCCCC

>ENA|AY665666|AY665666.1 Capra hircus MHC class II antigen (Cahi-DQA1)
 gene, Cahi-DQA1.6 allele, partial cds.

TGTTTGATAGTCAATTTCTTCTTTCACTGCTTAATGAAGATCTTTTCTCTATTTTTCCCT
 TTCTGGCTCCTCACCTGACTCAGCTGACCACATTGGCACCTATGGCATAAGCATCTACC
 AAACATATGGTCCCTCTGGCTACTATACCCATGAATTTGATGGAGATGAAGAGTTCTACG
 TGGACCTGGAAAAGAGGGAGACTGTCTGGCGTCTGCCTGAGTTTAGTAAATTTGCAAGTT
 TTGACCCTCAGGGTGCAGTCTGAGAAACATAGCCACGACAAAACATAATTTGAGAGTCTTGA
 TTCAAAGGTCCAACCTCTACTGCTGCTACCAACAGTATGTGTTTACCATTCTGCCTCTCTT
 TGTTGTTCTTCCCCAA

>ENA|L34082|L34082.1 Human (clone 96) MHC class II HLA-DQA1*0101 mRNA,
 partial cds.

GAAGACATTGTGGCTGACCACGTTGCCTCTTGTGGTGTAACCTGTACCAGTTTTACGGT
 CCCTCTGGCCAGTACACCCATGAATTTGATGGAGATGAGGAGTTCTACGTGGACCTGGAG
 AGGAAGGAGACTGCCTGGCGGTGGCCTGAGTTCAGCAAATTTGGAGGTTTTGACCCGCAG
 GGTGCACTGAGAAACATGGCTGTGGCAAAACACAACCTGAACATCATGATTAAACGCTAC
 AACTCTACCGCTGCTACCAATGAGGTTCTGAGGTACAGTGTTTTCCAAGTCTCCCCGTG
 AACTGGGTGAGCAATGGGAGTCACTGAGTACAGAGAGTGTCTGAGACCAGCTTC
 CTCTCCAAGAGTGATCATTCCTTCTTCAAGATCAGTTACCTCACCTTCTCCCTTCTGCT
 GATGAGATTTATGACTGCAAGGTGGAGCACTGGGGCCTGGACCAGCTCTTCTGAAACAC
 TGGGAGCCTGAGATTCCAGCCCCTATGTCAGAGCTCACAGAGACTGTGGTCTGCGCCCTG
 GGGTTGTCTGTGGGCCTCGTGGGCATTGTGGTGGGCACTGTCTTCATCATCCAAGGCCTG
 CGTTCAGTTGGTGCTTCCAGA

4.3 DQA2

Sheep

>ENA|AY312375|AY312375.1 Ovis aries MHC class II antigen (OLA-DQA2) gene,
 OLA-DQA2*0101 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAACAGCCTGGATTCTAACAGGACAGCTACCAGCACTGAGGGA
 GAAGGAAGCAGGTGCTGGCACTTTGCTTAGAGACATTGTGCCAAAGGTGAAGCCCACCGT
 GTTTGAAAGTTAGTCTCTTCTGTTACTTTGTTTAATATGGTCTTTTCTTCCCTCTGTTT

TCCACCTTCCTGCTCCTCACCCCTCACAGCTGACCACGTTGGCATCTATGGCGCAGACTTC
TACCAATCTCATGGTCCCTCTGGCCAGTACACCCACGAATTTGATGGGGACGAGCTGTTT
TATGTGGACCTGGGGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGGTGAATTCACA
AGTTTTGACCCGCAAGGTGCACTGAGTGAAATAGCTACAGCGAAACACAACTTGGATATC
ATGATTAAACGTTCCAACCTTTACCCCTGTTATCAATGGTAAGTGTCCACCATTCTACTTC
TCTTTACTGAATCTATTATTTTCATATCAGGCTTCACTCCCTTCTTCTCTAAGGAGAGATA
TCCTTCACCATGCTATGAAACTTTCCCGTGTCCCCAGATTTTCATAGTAATTATTGAACAC
TCATCCTCTCCCATCTCAAAGATCACATATTTCCATGTAATATAAGGACCCTTACTCCCA
TAACATATTCCCTGAATCCCTCAGGGAGGAGTCCCACAGACCTCCCTCCTTAACAAACAT
GCCCACAGACAGCACAGGGATAAAGCGTGGGCAGCGCATAGCATCTCCCAGCAGAAGGCA
AACAAGAGCTCCTCCTCTGTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312376|AY312376.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*0102 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAACAGCCTGGATTCTAACAGGACAGCTACCAGCACTGAGGGA
GAAGGAAGCAGGTGCTGGCACTTTGCTTAGAGACATTGTGCCAAAGGTGAAGCCCACCGT
GTTTGAAAGTTAGTCTCTTCTGTTACTTTGTTTAATATGGTCTTTTCTTTCCCTCTGTTT
TCCACCTTCCTGCTCCTCACCCCTCACAGCTGACCACGTTGGCATCTATGGCGCAGACTTC
TACCAATCTCATGGTCCCTCTGGCCAGTACACCCACGAATTTGATGGGGACGAGCTGTTT
TATGTGGACCTGGGGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGGTGAATTCACA
AGTTTTGACCCGCAAGGTGCACTGAGTGAAATAGCTACAGCGAAACAAAACCTTGGATATC
ATGATTAAACGTTCCAACCTTTACCCCTGTTATCAATGGTAAGTGTCCACCATTCTACTTC
TCTTTACTGAATCTATTATTTTCATATCAGGCTTCACTCCCTTCTTCTCTAAGGAGAGATA
TCCTTCACCATGCTATGAAACTTTCCCGTGTCCCCAGATTTTCATAGTAATTATTGAACAC
TCATCCTCTCCCATCTCAAAGATCACATATTTCCATGTAATATAAGGACCCTTACTCCCA
TAACATATTCCCTGAATCCCTCAGGGAGGAGTCCCACAGACCTCCCTCCTTAACAAACAT
GCCCACAGACAGCACAGGGATAAAGCGTGGGCAGCGCATAGCATCTCCCAGCAGAAGGCA
AACAAGAGCTCCTCCTCTGTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312377|AY312377.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*0103 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAACAGCCTGGATTCTAACAGGACAGCTACCAGCACTGAGGGA
GAAGGAAGCAGGTGCTGGCACTTTGCTTAGAGACATTGTGCCAAAGGTGAAGCCCACCGT
GTTTGAAAGTTAGTCTCTTCTGTTACTTTGTTTAATATGGTCTTTTCTTTCCCTCTGTTT
TCCACCTTCCTGCTCCTCACCCCTCACAGCTGACCACGTTGGCATCTATGGCGCAGACTTC
TACCAATCTCATGGTCCCTCTGGCCAGTACACCCACGAATTTGATGGGGACGAGCTGTTT
TATGTGGACCTGGGGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGGTGAATTCACA
AGTTTTGACCCGCAAGGTGCACTGAGTGAAATAGCTAAAGCAAAAACAAACCTTGGATATC
ATGATTAAACGTTCCAACCTTTACCCCTGTTATCAATGGTAAGTGTCCACCATTCTACTTC
TCTTTACTGAATCTATTATTTTCATATCAGGCTTCACTCCCTTCTTCTCTAAGGAGAGATA
TCCTTCACCATGCTATGAAACTTTCCCGTGTCCCCAGATTTTCATAGTAATTATTGAACAC
TCATCCTCTCCCATCTCAAAGATCACATATTTCCATGTAATATAAGGACCCTTACTCCCA
TAACATATTCCCTGAATCCCTCAGGGAGGAGTCCCACAGACCTCCCTCCTTAACAAACAT
GCCCACAGACAGCACAGGGATAAAGCGTGGGCAGCGCATAGCATCTCCCAGCAGAAGGCA
AACAAGAGCTCCTCCTCTGTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312378|AY312378.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*0201 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAGCAGCCCGGATTCTAACAGGACAGCTACCAACACTGAGGGG
AAAGGAAGCCGATACTGGGAATTTTGCTTAAAGACTTTGTGCTAAAGATGAACCCACAG
TCTTTGAAAGTTAGTCTCTTCTGTTATTTTGTGTTAACATGTTCTTTCCCTCTGTTTCCA
CCCTCCTTCTCCTCACCCCTCACTGACAGCTGACCACATTGGCATCTACGGCGCAGACTTC
TACCAATCTCATGGTCCCTCTGGCCAGTACATCCATGAATTTGATGGAGATGAGCAGTTT
TATGTGGACCTGGAGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGGTGAATTAACA
AGTTTTGACCCGCAAGGTGCACTGAGTGAAATAGCTACATCAAAAACAAAACCTTGGATATC
ATGATTAAACGTTCCAACCTTTACCCAGTTATCAACGGTAAGTGTCCACCATTCTACTTC
TCTTTACTGAATCTATTCTTTTCATATCAGGCTTCACTCCCTTCTTCTCTAAGGAGAGATA
TCCTTCACCAAGCTATGAAACTTTCCCAAGTGTCCCCAGATTTTCATAGTAATTATTGACC
ACTCATCCTCTCCCATCTCAAAGATCACATATTTCCATGTAATATAAGGACCCTTACTCC
CATAACATATTCCCTGAATCCCTCAAGGAGGAGTCCCACAGACCTCCTCCTTAACAAGCA
TGCCCACAGACAGCACAGGGATAAAGCGCAGGCAGCGCATAGCATCTCCCAGCAGAAGGC
AAACAAGAGCTCCTCCTCTGTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312379|AY312379.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene, OLA-DQA2*0301 allele, exon 2 and partial cds.
CACATGTTACAGTGCAAAAACAGCCTGGATTCTAACAGGACAGCTACCAGCACTGAGGGA
GAAGGAAGCAGGTGCTGGCACTTTGCTTAGAGACATTGTGCCAAAGGTGAAGCCACCGT
GTTTGAAAGTTAGTCTCTTCTGTTACTTTGTTAATATGGTCTTTTCTTTCCCTCTGTTT
TCCACCTTCTGCTCCTCACCTTCACAGCTGACCACGTTGGCATCTACGGCGCAGAATTC
TACCAATCTCATAGTCCCTCTGGCCAGTACACCCACGAATTTGATGGAGACGAGCTGTTG
TATGTGGACCTGGAGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGGTGAATTAACA
AGTTTTGACCCACAAGGTGCACTGAGTAACATAGCTACAGAGAAAACAACTTGGATATC
ATGATTAAACGTTCCAACCTTTACCCCTGTTATCAATGGTAAGTGTCCACCATTCTACTTC
TCTTTACTGAATCTATTCTTTTCATATCAGGCTTCACTCCCTTCTTCTCTAAGGAGAGATA
TCCTTCACCATGCTATGAACTTTCCCAAGTTGCCCCAGATTTTCATAGTAATTATTGAAC
ACTCATCCTCTCCCATCTCAAAGATCACATATTTCCATGTAATATAAGGACCTTACTCC
CATAACATATTCTTGAATCCCTCAGGGAGGAGTCCCACAGACCTCCCTCCTTAAGAAGC
ATGCCACAGACAGCACAGGGATAAAGCGTGGGCAGCGCATAGCATCTCCCAGCAGAAGG
CAAACAAGAGCTCCTCCTCTGTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312380|AY312380.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene, OLA-DQA2*0501 allele, exon 2 and partial cds.
CACATGTTACAGTGCAAAAAGCAGCCCGATTCTAACAAAGACAGCTACCAACACTGAGGGG
AAGGAAGCCGATACTGGGAATTTTGCTTAGAGACTTTGTGCTAAAGATGAACCCACAG
TCTTTGAAAGTTAGTCTCTTCTGTTACTTTGTTAATATGGTCTTTTCTTTCCCTCTGTT
TTCCACCTTCTGCTCCTCACCTCACTTATCAGCTGACCACGTTGGCTGCTATAGCACA
ATTATCTACCAATCTCATGGTCCCTCTGGCCAGTTCACCCATGAATTTGATGGAGACGAG
TTGCTTTATGTGGACCTTGAGAAGAAGGAGACTGTCTGGCGGCTGCCTATTTTTGGTGAA
TTAACAAGTTTTGACCCGCAAGGTGCACTGAGTAACATAGCTACAGCGAAAACAACTTG
GATATCCTGACTAAATGCTCCAATTGTACCCAGTTATCAACGGTAAGTGTCCACCATTCT
TACTTCTCTTTACTGAATCTATTCTTTTCATATCAGGCTTCACTCCCTTCTTCTCTAGGGA
GAGATATCCTTCACCACTCTATAAACTTTTCCAAGAGTGCCAGGTTTCATAGTAATTA
TTGACCACTCATCCTCTCCCATCTCAAAGATCACATATTTCCATGTAATATAAGGACCTT
TACTCCCATAACATATTCTTGAATCCCTCAAGGAGGAGTCCCACAGACCTCCCTCCTTA
ACAAGCATGCTCACAGACCGCACGGGGATAAAGCGTGGGCAGCGCATAGCATCTCCCAGC
AGAAGGCAAACAAGAGCTCCTCCTCTGTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312381|AY312381.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene, OLA-DQA2*0601 allele, exon 2 and partial cds.
CACATGTTACAGTGCAAAAACAGCGAGGATTCTAACAGGACAGCTACCAACACTGAGGGA
GAAGGAAGCCGATACTGGGAATTTTGCTTAGAGACTTTGTGCTAAAGATGAACCCCGCAG
TCTTTGAAAGTTAGTCTCTTCTACTTTTTTAAATATGTTCTTTCTCTCTGTTTTCCACTT
TCCTGCTTCTCACCTCACTTATCAGCTGACCACGTTGGCACCTATGGCGCAGAATTCCTA
CCAATCTCATGGTCCCTCTAGCGAGTACACCCAGGAATTTGACGAAGACGAGCTGCTTTA
TGTGGACCTGGAGAAGAAAGAGACTGTCTGGCGGCTGCCTATGTTTGGCCAGTTTGCAGG
TTTTTCACATTCAAGTTGCACTGAGTAACATAGCTACAGCGAAAACAACTTGGATGTCAT
GACTAAATGGTACAACCTTTACCCAGTTATCAATGGTAAGTGTCCACCATTCTACTTCTC
TTTCTGAATCTATTCTTTTCATATCAGGCTTCACTCCCTTCTTCTCTAAGGAGGGATATC
CTTCACCACTCTATGAACTTTTCCAAGGGTCCCCAGGTGTCATAGTAATTATTGACCAC
TCATCCTCTCCCATCTCAAAGATCACATATTTCCATGTAATATAAGGACCTTACTCCCA
TAACATATTCTTGAATCCCTCAAGGAGGAGTCCCACACGCCTCCCTCCTTAACAAGCAT
GCCACAGACAGCACGGGGATAAAGCGTGGGCAGAGTATAGCATCTCCCAGCAGAAGGCA
AACAGAGCTCCTCCTCCTCTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312382|AY312382.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene, OLA-DQA2*0602 allele, exon 2 and partial cds.
CACATGTTACAGTGCAAAAACAGCGAGGATTCTAACAGGACAGCTACCAACACTGAGGGA
GAAGGAAGCCGATACTGGGAATTTTGCTTAGAGACTTTGTGCTAAAGATGAACCCCGCAG
TCTTTGAAAGTTAGTCTCTTCTACTTTTTTAAATATGTTCTTTCTCTCTGTTTTCCACTT
TCCTGCTTCTCACCTCACTTATCAGCTGACCACGTTGGCACCTATGGCGCAGAATTCCTA
CCAATCTCATGGTCCCTCTAGCGAGTACACCCAGGAATTTGACGAAGACGAGCTGCTTTA
TGTGGACCTGGAGAAGAAAGAGACTGTCTGGCGGCTGCCTATGTTTGGCCAGTTTGCAGG
TTTTTCACATTCAAGTTGCACTGAGTAACATAGCTACAGAGAAAACAACTTGGATGTCAT
GACTAAATGGTACAACCTTTACCCAGTTATCAATGGTAAGTGTCCACCATTCTACTTCTC
TTTCTGAATCTATTCTTTTCATATCAGGCTTCACTCCCTTCTTCTCTAAGGAGGGATATC
CTTCACCACTCTATGAACTTTTCCAAGGGTCCCCAGGTGTCATAGTAATTATTGACCAC
CTTCACCACTCTATGAACTTTTCCAAGGGTCCCCAGGTGTCATAGTAATTATTGACCAC

TCATCCTCTCCCATCTCAAAGATCACATATTTCCATGTAATATAAGGACCCTTACTCCCA
TAACATATTCCCTTGAATCCCTCAAGGAGGAGTCCCACACGCCTCCCTCCTTAACAAGCAT
GCCCACAGACAGCACGGGGATAAAGCGTGGGCAGAGTATAGCATCTCCCAGCAGAAGGCA
AACAAGAGCTCCTCCTCTCTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312383|AY312383.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*0701 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAACAGCCCGGATTCTAACAGGACAGCTACCAACACTGAGGGG
AAAGGAAGCCGATACTGGGAATTTTGCTTAGAGACTTTGTGCTAAAGATGAACCCACAG
TCTTTGAAAGTTAGTCTCTTCTGTTACTTTGTTTAATACGGCCTTTTTCTCCATTTTCC
ACCTTCCTGCTCCTCACCTCACTTACAGCTGACCACGTTGGCTCCTATGGCACAGTTAT
CTACCAATCTCATGGTCCCTCTGGCCAGTACACCCATGAATTTGATAGAGACGAGCTGTT
TTATGTGGACCTGGAGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTAGCCAGTTTGC
AGGTTTTTGACCCTCAAGGTGCACTGAGTAACATAGCTACAGCGAAACACAACCTTGGATAT
CATGACTCAATGGCACAACCTCTACCCCAGTTATCAATGGTAAGTGTCCACCATTCTGCTT
CTCTTTACTGAATCTATTCTTTTCATATCAGGCTTCACTCCCTTCTTCTCTAAGGAGAGAT
ATCCTTCACCACGCTATGAAACTTTTCCAAGAGTCCCCAGGTTTCATAGTAATTATTGAC
CACATGTCCTCTCCCATCTCAAAGATCACATATTTCCATGTAATATAAGGACCCTTATTC
CCATAACATATTTCCTTGAATCCCTCAAGGAGGAGTCCCACAGACCTCCCTCCTTAACAAG
CATGACCACAGACAGCATGGGGATAAAGCATGGGCAGAGCATAGCATCTCCCAGCAGAAG
GCAACAAGAGCTCCTCCTCTGTCTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312384|AY312384.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*0702 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAAGCAGCCCGGATTCTAACAGGACAGCTACCAACACTGAGGGG
AAAGGAAGCCGATACTGGGAATTTTGCTTAGAGACTTTGTGCTAAAGATGAACCCACAG
TCTTTGAAAGTTAGTCTCTTCTGTTACTTTGTTTAATTCGGCCTTTTTCTCTCCATTTTCC
ACCTTCCTGCTCCTCACCTCACTTACAGCTGACCACGTTGGCTCCTATGGCACAGTTAT
CTACCAATCTCATGGTCCCTCTGGCCAGTACACCCATGAATTTGATAGAGACGAGCTGTT
TTATGTGGACCTGGAGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTAGCCAGTTTGC
AGATTTTTGACCCTCAAGGTGCACTGAGTAACATAGCTACAGCGAAACACAACCTTGGATAT
CATGACTCAATGGCACAACCTCTACCCCAGTTATCAATGGTAAGTGTCCACCATTCTGCTT
CTCTTTACTGAATCTATTCTTTTCATATCAGGCTTCACTCCCTTCTTCTCTAAGGAGAGAT
ATCCTTCACCACGCTATGAAACCTTTTCCAAGAGTCCCCAGGTTTCATAGTAATTATTGAC
CACATGTCCTCTCCCATCTCAAAGATCACATATTTCCATGTAATATAAGGACCCTTATTC
CCATAACATATTTCCTTGAATCCCTCAAGGAGGAGTCCCACAGACCTCCCTCCTTAACAAG
CATGACCACAGACAGCATGGGGATAAAGCATGGGCAGAGCATAGCATCTCCCAGCAGAAG
GCAACAAGAGCTCCTCCTCTGTCTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312385|AY312385.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*08011 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAACAGCCTGGATTCTAACAGGACAGCTACCAACACTGAGGGG
AAAGGAAGCCAATACTGGGAATTTTGCTTAGAGCTTTGTGCTAAAGATGAACCCCGCAGT
CTTTGAAAGTTAGTCTCTTCTGTTACTTTGTTTAATATGTTCTTTCTCTCTGTTTTCCAC
CTTCCTGCTCCTCACCTCACTTACAGCTGACCACCTTTGGCTCCTATGGCACAACCTATCT
ACCAATCTCATGGTCCCTCTGGCCAGTTCACCCAGGAATTTGACGGAGATGAGCTGTTTT
ATGTGGACCTGGAAAAGAAAGAGACTGTCTGGCGGCTGCCTATGTTTAGCCAGTTTGCAG
GTTTTTGACCCTCAAGGTGCACTGAGTAACATAGCTGCAGCGAAACACAACCTTGGATATCC
TGACTAAACGCTCCAACCTCTACCCCAGTTATCAACGGTAAGTGTCCACCATTCTACTTCT
CTTTACTGAATCTATTCTTTTCATATCAGGCTTCACTCCCTTCTTCTCTAAGGAGAGATAT
CCTTCACCATGCTATGAAACTTTCCCAAGTTGCCCCAGATTTTCATAGTAATTATTGACCA
CTCATCCTCTCCCATCTCAAAGATCACGTATTTCCATGTAATATAAGGACCCTTACTCCC
ATAGCATATTTCCTTGAATCCTTCAAGGAGGAGTCCCACAGACCTCCCTCCTTAACAAGCA
TGACCACAGACAGCATGGGGATAAAGCGTGGGCAGAGCATAGCATCTCCCAGCAGAAGGC
AAACAACAGCTCCTCCTCTGTCTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312386|AY312386.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*08012 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAACAGCCTGGATTCTAACAGGACAGCTACCAACACTGAGGGG
AAAGGAAGCCAATACTGGGAATTTTGCTTAGAGACTTTGTGCTAAAGATGAACCCCGCAG
TCTTTGAAAGTTAGTCTCTTCTGTTACTTTGTTTAATATGTTCTTTCTCTCTGTTTTCCA
CCTTCCTGCTCCTCACCTCACTTGCAGCTGACCACCTTTGGCTCCTATGGCACAACCTATC
TACCAATCTCATGGTCCCTCTGGCCAGTTCACCCAGGAATTTGACGGAGATGAGCTGTTT

TATGTGGACCTGGAAAAGAAAGAGACTGTCTGGCGGCTGCCTATGTTTAGCCAGTTTGCA
GGTTTTGACCCTCAAGGTGCACTGAGTAACATAGCTGCAGCGAAACACAACCTTGATATC
CTGACTAAACGCTCCAACCTCTACCCAGTTATCAACGGTAAGTGTCCACCATTCTACTTC
TCTTTACTGAATCTATTCTTTTCATATCAGGCTTCACTCCCTTCTTCTCTAAGGAGAGATA
TCCTTCACCATGCTATGAAACTTTCCCAAGTTGCCCCAGATTTCATAGTAATTATTGACC
ACTCATCCTCTCCCATCTCAAAGATCACGTATTTCCATGTAATATAAGGACCCCTACTCC
CATAGCATATTCCCTGAATCCCTCAAGGAGGAGTCCCACAGACCTCCCTCCTTAACAAGC
ATGACCACAGACAGCATGGGGATAAAGCGTGGGCAGAGCATAGCATCTCCCAGCAGAAGG
CAAACAACAGCTCCTCCTCTGTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312387|AY312387.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*0901 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAACAGCCTGGATTCTAACAGGACTGCTACCAGCACTGAGGGG
AAAGGAAGCTGATACTGGGAATTTTGCTTAGAGACTTTGTGCTAAAGATGAAGCCCACAG
TCTTTGAAAGTTAGTCTCTTCTGTTACTTTGTTTAATATGTTCTTTCCCTCTCTTTTCCA
CCTTCCTGCTCCTCACCCCTCACTTATCAGCTGACCACATTGGCTCCTATGGCACAACATAT
CTACCAATCTCATGGTCCCTCTAGCCAGTACACCCAGGAATTTGATGGAGACGAACTGTT
TTATGTGGACCTGGAGAAGAAGGAGACCGTCTGGCGGCTGCCTATGTTTAGCCAGTTTGC
AGGTTTTTAACATTCAAGATGCACTGAATAACATACCTGCAGCGAAACACAACCTGGGTAT
CCTGACTAAACGCTCCAACCTTTACCCAGTTATCAACGGTAAGTGTCCACCATTCTACTT
CTCTTTACTGAATCTATTCTTTTCATATCAGGCTTCGCTCCCTTCTTCTCTAAGGAGGGAT
ATCCTTCACCACTCTATGAACTGTTCCAAGTGTCCCCAGATTTCATAGTAATTATTGAA
CATTCGTCCTCTCCCATCTCAAAGATCACATATTCCATGTAATATAAGGACTCTTACTCC
CATAACATATTCCCTGAATCCCTCAAGGAGGAGTCCCACAAACCTCCTCCTTAACAAGCA
TGCCCCACAGACAGCATGGGGATAAAGCATGGGCAACGTATTGCATCTCCAGGCAGAAGGC
AAACAAGAGCTCCTCCTCTGTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312388|AY312388.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*1001 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAACAGCCCGGATTCTAACAGGACAGCTACCAACACTGAGGGG
AAAGGAAGCCGATACTGGGAATTTTGCTTAGAGACTTTGTGCTAAAGGTGAACCCCACAG
TCTTTGAAAGTTAGTCTCTTCTGTTACTTTGTTTAATATGGCCTTTTCTCTCCATTTTCC
ACCTTCTTGCTCCTCACCCCTCACTTACAGCTGACCACGTTGGCTCCTACGGCACAGACTT
CTACCAATCTCATGGTCCCTCTGGCCAGTTACACCCAGGAATTTGATGGAGACGAGTTGCT
TTATGTGGACCTGGGGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTAGCCAGTTTGC
AGATTTTGACCCTCAAGGTGCACTGAGGAACATAGCTACAGCAAAAGACACCTTGATAT
CCTGACTAAACGCTCCAACCTCTACCCAGTTATCAATGGTAAGTGTCCACCATTCTACTT
CTCTTTACTGAATCTATTCTTTTCATATGAGGCTTCACTCCCTTCTTTAAGAAGAGATATC
CTTCACCACCTCTATAAAACCTTTTCCAAGAGTCCCCAGATTTCATAGTAATTATTGAACAC
TCATCCTCTCCCATCTCAAAGATCACATATTTCATGTAATATAAGGACCTTACTCCCA
TAACATATTCCCTGAATCCCTCAAGGAGGAGTCCCACAGACCTCCTCCTTAACAAGCATG
CCCACAGACAGCACGGGGATAAAGCGTGGGCAGAGCATAGCATCTCCCAGCAGAAGGCCAA
ACAAGAGCTCCTCCTCTGTCGGAAGTGGGAAACGTTGGTGAGAGGG

>ENA|AY312389|AY312389.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*1101 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAGCAGCCTGGATTCTAACAGGACAGCTACCAGCACTGAGGGA
GAAGGAAGCAGGTGCTGGCACTTTGCTTAGAGACATTGTGCCAAAGGTGAAGCCCACCGT
GTTTGAAAGTTAGTTTCTTCCGTTACTTTGTTTAATATGGCCTTCTCTCTCCATTTTCCA
CCTTCCTGCTCCTCACCCCTCACTTACAGCTGACCACCTTTGGCTCCTATGGCATAACATGTC
TACCAATCTCATGGTCCCTCTGGCCAGTACACCCATGAATTTGATGGAGACGAGCTGTTT
TATGTGGACCTGGGGAAGAAGGAGACAGTCTGGCGGCTGCCTATGTTTAGCCAGTTTGC
GGTTTTGACCCACAGCGTGCACTGATTCAATTAGCTACATCGAAGCACAACCTTGATTAC
ATGACTAAACACTCCAACCTTTACCCATGCCATCAACGGTAAGTGTCCACCATTCTACTTC
TCTTCTCTGAATCTATTCTTTCTTATCAGGCTTCACTCTCTTCTTCTCTAAGGAGAGATA
TCCTTCAACCACTCTATGAACTTTTCCAAGAGTCCCCAGATTTCATAGTAATTACTGAAC
ACTCAGTCTCTCCCATCTCAAACATCACATATTTCATGTAAGGTACTTACTCCCATAA
CATATTCTTGAATCCCTCAAGGAGGAGTCCCACAGACCTCCCTCCTTGACAAGCATTCC
CACAGACAGCACGGGGATAAAGCGTGGGCAGCGCATAGCATCTCCCAGCAGAAGGCCAAAC
AAGAGCTCCTCCACTGTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312390|AY312390.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*1201 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAACAGCCTGGATTCTAACAGGACAGCTACCAACACTTAGGGA
AAAGGAAGCAGGTGCTGGCACTTTGCTTAGAGACATTGTGCCAAAGGTGAAGCCCACCGT
GTTTGAAAGTTAGTCTCTTCTCAGCTACTTTGTTTAAATATGGCCTTTTCTCTCTGTTTTCCA
CCTTCCTGCTCCTCACCCTCACTTATCAGCTGACCACTTTGGCTCCTATGGCAGAGAT
CTACCAATCTCATGGTCCCTCTGGCCAGTACACCCAGGAATTTGATGGAGACGAGCTGTT
TTATGTGGACCTGGGGAAGAAGGAGACTGTCTGGAGGCTGCCTATGTTTAGCCAGTTTGC
AGGTTTTGATCCACAGGGTGCAGTGAATAGCTACAGCAAAAACAAAACCTTGGATAT
CCTGACTAAACGCTCCAACCTTTACCCCTGCTATCAATGGTAAGTGTCCACCATTCTACTT
CTCTTTACTGAATCTATTCTTTTCATATCAGGCTTCACTCCCTTCTTTTCTAAGGAGAGAT
ATCCTTACCATGCTATGAACTTTCCCAAGTGTCCCCAGATTTTCATAGTAATTATTGAA
CACTCATCCTCTCCACCTCAAAGATCACATATTTCCATGTAATATAAGGACCCTTACTC
CCATAACATATTCCCTTGAATCCCTCAAGGAGGAGTCCCACAGACCTCCTCCTTAACAAGC
ATGCCACAGACAGCACGGGGATAAAGCATGGGCAACATATAGCATCTCCAGCAGAAGG
CGAACAAGAGCTCCTCCTCTGTCTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312391|AY312391.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*1301 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAACAGCCTGGATTCTAACAGGACAGCTACCAACACTGAGGGG
AAAGGAAGCCGATACTGGGAATTTTGTCTTAGAGACTTTGTGCTAAAGATAAACCCACAG
TCTTTGAAAGTTAGTCTCTTCTGTTACTTTGTTTAAATATGGTCTTTTCTTTCCCTCTGTT
TTCCACCTTCTGCTCCTCACCCTCACTGATAGCTGACCACTTGGCACCTACGGCAGCAG
ACTTCTACCAATCTCATGGTCCCTCTGGCGAGTACATCCACGAATTTGATGGAGACGAGC
AGCTTTTATGTGGACCTGGAGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGATGGAT
TAAGTTTTTGACCCACAGCGTGCACTGAGTAACATAGCTATAGCGAAAACACAACCTTGAATA
TCCTGACTAAACGCTACAACCTTTACCCAGTTATCAACGGTAAGTGTCCACCATTCTACT
TCTCTTTACTGAATCTATTCTTTTCATATCAGGCTTCACTCCCTTCTTCTCTAAGGAGAGA
TATCCTTACCACCTCTATAAACTTTTCCAAGAGTCCCCAGATTTTGTAGTAATTATTGAA
CCACTCATCCTCCCCATCTCAAAGATCACATATTTCCATGTAATATAAGGACCCTTACT
CCCAAAACATATTCCCTTGAATCCCTCAAGGAGGAGTCCCACAAACCTCCCTCCTTAAAAA
AGCATGCCCCGAGACAGCATGGGGATAAAGCGTGGGCAGCGCATAGCATCTCACAGCAGA
AGGCAACAAGAGCTCCTCCTCTGTCTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312392|AY312392.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*1401 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAACAGCCTAAATTCTAACAGGACAGCTACCAACACTCAGGGG
AAAGGAAGCCGATACTGGGAATTTTGTCTTAGAGACTTTGTGCTAAAGATGAACCCACAG
TCTTTGAAAGTTAGTCTCTCTGTTACTTTGTTTAAATATGGTCTTTTCTTTCCCTCTGTT
TTCCACCTTCTGCTCCTCACCCTCACTTATCAGCTGACCACATTGGCACCTACGGCACA
GACTTCTACCAATCTCATGGTCCCTCTGGCCAGTACATCCACGAATTTGATGGAGACGAG
CAGCTTTTATGTGGACCTGGAGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGATGGA
TTAAGTTTTTGACCCACAGCGTGCACTGAGTAACATAGCTATAGCGAAAACACAACCTTGGAT
AGGCTGACTAAATGGTACAACCTTTACCCAGTTATCAACGGCAAGTGTCCACCATTCTAC
TCCTCTTTACCGAATCTATTCTTTTCATGTCTCAGGCTTCACTCCCTTCTTCTCTAAGAAGAG
ATGTCCTTACCACCTCTATAAACTTTTCCAAGAGTACCAGATTTTGTAGTAATTATTG
ACCACTCATCCTCTCCCATCCCAAAGATCACATATTTCCATGTAATACAAGCACCTTAC
TCCCATAAACATATTCCCTTGAATCCCTCAAGGAGGAGTCCCACAGACCTCCCTCCTTAACA
AGCATGCCCACAGAAAGCACGGGGATAAAGCATGGGCAATGTATAGCATCTCCAGCAGA
AGGCAACAAGAGCTCCTCCTCTGTCTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312393|AY312393.1 *Ovis aries* MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*1501 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAACAGCCTAAATTCTAACAGGACTGCTACCAACACTGAGGGG
AAAGGAAGCCGATACTGGGAATTTTGTCTTAGAGACTTTGTGCTAAAGATGAACCCACAG
TCTTTGAAAGTTAGTCTCTTCTGTTATTTTGTAAATATGGTCTTTTCTTTCCCTCTGTT
TTCCACCTTCTGCTCCTCACCCTCACTTATCAGCTGACCACGTTGGCATCTATGGCACA
GACTTCTACCAATCTCATGGTCCCTCTGGCGAGTACATCCACTTATTTGATGGAGACGAA
GAGTTTTTATGTGGACCTGGAGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGATGAA
TTAAGAAGATTTTGACCCGCAAGGTGCACTAAATAACATAGCTATAGCGAAAACACAACCTG
GATATCCTGACTAAACGCTACAACCTTTACCCAGTTATCAACGGTAAGTGTCCACCATTCT
TGCTTCTCTTTACTGAATCTATTCTTTTCATATCAGGCTTCACTCCCTTCTTCTCTAAGGA
GAGATATCCTTACCACCTCTATAAACTTTTCCAAGAGTCCCCAGATTTTGTAGTAATTATA
TTGACCACTCATCCTCTCCACCTCAAAGATCACATATTTCCATGTAATATAAGGACCCT
TACTCCCAAAACATATTCCCTTGAATCCCTCAAGGAGGAGTCCCACAAACCTCCCTCCTTG

ACAAGCATGCCCACAGACAGCACAGGGATAAAGTGTGGGCAGAACATAGCATCTCCCAGC
AGAAGGCCAAACGAGCTCCTCCTCTGTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312394|AY312394.1 Ovis aries MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*1601 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAACAGCCTGGATTCTAACAGGACAGCTACCAACACTGAGGGG
AAAGGAAGCCGATACTGGGAATTTTGCTTAGAGACTTTGTGCTAAAGATAAACCCACAG
TCTTTGAAAGTTAGTCTCTTCTGTTACTTTGTTAATATGGTCTTTTCTTCCCTCTGTT
TTCCACCTTCCTGCTCCTCACCTCACTGATAGCTGACCACGTTGGCACCTACGGCACAG
ACTTCTACCAATCTCATGGTCCCTCTGGCGAGTACATCCACGAATTTGATGGAGACGAGC
TGTTTTATGTGGACCTGGGGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGGTGAAT
TGACAAGTTTTGACCCACAAGGTGCACTGAGTAATATAGCTATAGCAAAACACAACCTTGA
ATATCCTGACTAAACGCTACAACTTTACCCAGTTATCAATGGTAAGTGTCCACCATTCT
ACTTCTCTTTACTGAATCTATTCTTTTCATATCAGGCTTCACTCCCTTCTTCTTAAGGAG
AGATATCCTTCACCACTCTATAAACTTTTCCAAGAGTCCCCAGATTTTGTAGTAATTAT
TGACCACTCATCTCCCCATCTCAAAGATCACATATTTCCATGTACTATAAGGACCCCTT
ACTCCCAAACATATTCTTGAATCCCTCAAGGAGGAGTCCCAAAAACCTCCCTCCTTAA
AAAAGCATGCCCCGAGACAGCATGGGGATAAAGCGTGGGCAGCGCATAGCATCTCACAGC
AGAAGGCCAAACGAGCTCCTCCTCTGTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312395|AY312395.1 Ovis aries MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*1701 allele, exon 2 and partial cds.

CACATGTTACAGTGCAAAAACAGCCTAAATTCTAACAGGACAGCTACCAACACTGAGGGG
AAAGGAAGCCGATACTGGGAATTTTGCTTAGAGACTTTGTCTAAAGATGAAGCCCACCA
TGTTTTGAAAGTTAGTCTCTTCTGTTACTTTGTTAATATGGTCTTTTCTTCTCTCCGTT
TTCCACCTTCCTGGTCTCACCCTCACTGACAGCTGACCACGTTGGCACCTACGGCACAA
ACTTCTACCAATCTCATGGTCCCTCTGGCCAGTATATCCACTTATTTGATGGAGACGAGC
GGTTTTATGTGGACCTGGAGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGGTGAAT
TAATAAGTTTTGACCCACAAGGTGCACTGAGTAACGTAGCTGCATCGAAACACAACCTTGG
ATATCCTGACTAAACGCTCCAACTTTACCCCTGTTATCAATGGTAAGTGTCCACCATTCT
GCTTCTCTTTACTGAATCTATTCTTTTCATATCAGGCTTCACTCCCTTCTTCTTAAGGAG
AGATATCCTTCACCATGCTATGAAACTTTTCCAAGAGTCCCCAGGTTTCACAGTAATTAT
TGAACACTCATCTTCTCCCATCTCAAAGATCACATATTTCCATGCAATATAAGGACCCCTT
ACTCCATAACATATTCCCTGAATCCCTCAAGGAGGAGTCCCAACAGACCTCCTCCTTAAG
AAGCATTTCCACAGACAGCATGGGGATAAAGCGTGGGCAGCGCATAGCATCTCCCTGCAG
AAGGCCAAACAAGAGCTCCTCCTCTGTCAGACTGGGAAACGTTGGTGAGAGGG

>ENA|AY312396|AY312396.1 Ovis aries MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*0401 allele, exon 2 and partial cds.

ACTACCAATCTCATGGTCCCTCTGGCCAGTACACCATGGAATCTGATGGAGACGAGCTGT
TTTATGTGGACCTGGAGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGGTGAATTAA
CAAGTTTTGACCCGCAAGGTGCACTGAGTGAAATAGCTAAAGCAAAACAAAACCTTGGATA
TCCTGACTAAACTCTCCAACCTTACCCCTGTTATCAATGGTAAGTGTCCACCATTCTACT CC

>ENA|AY312397|AY312397.1 Ovis aries MHC class II antigen (OLA-DQA2) gene,
OLA-DQA2*0402 allele, exon 2 and partial cds.

ACTACCAATCTCATGGTCCCTCTGGCCAGTACACCATGGAATCTGATGGAGACGAGCTGT
TTTATGTGGACCTGGAGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGGTGAATTAA
CAAGTTTTGACCCGCAAGGTGCACTGAGTGAAATAGCTAAAGCAAAACAAAAGCTTGGATA
TCCTGACTAAACTCTCCAACCTTACCCCTGTTATCAATGGTAAGTGTCCACCATTCTACT CC

Cattle

>ENA|D50045|D50045.1 Bos taurus mRNA for MHC class II DQA2, complete cds.

CTCAGAACAGCCACTGGTGAGTCCACCTTGAGAAGAGGATGGTCTGAACAGAGCTCTGA
TTCTAGGGGCCCTCGCCCTGACCACCATGATGAGCTCCAGTGAGGTGAAGACATTGTGGCTGACCACGTTGG
CTCCTATGGCAGAGATCTACCAATCTCATGGTCCCTCTGGCCAGT
ACACCCAGGAATTTTGATGGAGACGAGATGTTTTATGTGGACCTGGGGAAGAAGGAGACTG
TCTGGAGGCTGCCTATGTTTAGCCAGTTTGCAGGTTTTGACCCACAGGCTGCACTGAGTG
AAATAGCTACAGCAAAACACAACCTTGGATGTCTGACTAAACGCTCCAACCTTACCCCTG
TTATCAATGAGGTTCCAGAGGTGACTGTGTTTTCCAAGTCTCCCGTATGCTGGGTCAGC
CCAACACCCTCATCTGTCACGTGGACAACATTTTTCCCCCTGTGATCAACATTACATGGC
TGAAGAACGGGCATGCAGTCACAGAGGGTGTCTGAGACCAGCTTCCTCCCTAAGGATG
ATCATTCTTTCTCAAGATTGGTTATCTCACCTTCCTCCCTCTGATAATGACATTTATG

ACTGCAAAGTGGAGCACTGGGGTCTGGATGAGCCACTTCTGAAACACTGGGAGCCTGAGG
 TTCCAGCCCCCTATGTCTAGAGCTGACAGAGACTGTGGTCTGTGCCCTGGGGTTGACCGTGG
 GCCTTGTGGGTATCGTGGTGGGCACCATCTTCATCATCCAAGGCCTGCGCTCAGGTGGGG
 CCTCCAGACACCAGGGTCCCTTGTGAGTCGCACCCTAGAAAGGAAGGTGCTCTGCCGATC
 TATGAGAGCAGAAGAGTGGACGTGCTAGACGACCTAGAACTAGTTTCTGGCAAAGTTTCAT
 CATATACTCTCTCTTCCCTGATACTCTGCCCCCTCCTCTCTTCTCTGGGACTTAAGATGCT
 GTATCATTTTCAGAGCTCACATATACCTCAGAGTTCTCCCCTGACTTTCTGATATTTTTTTT
 CTGTTCTCAGTAGTTGCCTACCATGAGATCACTGGGGTATTCCACCCTACTACTCACCCA
 GGTTGGAGTGAGTTACCTACCTACCACCCTAGTGACCTTGACCCCGTATTGCCATGGAAG
 CAATAAACTCCTCTTTAATAGAAAAAAAAAAAAAAAAAAAAAACTTTAGAGCACA

>ENA|D50046|D50046.1 Bos taurus BoLA-DQA2 mRNA for MHC class II DQA2,
 partial cds, clone: AQ16-1.

CTATGTTTtagccagtttgcaggttttgacccacaggctgcaactgagtgaaaatagctacag
 CAAAACACAACCTTGGATGTCTCTGACTAAACGCTCCAACTTTACCCCTGTTATCAATGAGG
 TTCCAGAGGTGACTGTGTTTTTCCAAGTCTCCCGTGATGCTGGGTGAGCCCAACACCCCTCA
 TCTGTCTACGTGGACAACATTTTTTCCCCCTGTGATCAACATTACATGGCTGAAGAACGGGC
 ATGCAGTCTACAGAGGGTGTCTCTGAGACCAGCTTCCTCCCTAAGGATGATCATTCTTTCC
 TCAAGATTGGTTATCTCACCTTCCTCCCTTCTGATAATGACATTTATGACTGCAAAGTGG
 AGCATGGGGTCTGGATGAGCCACTTCTGAAACACTGGGAGCCTGAGGTTCCAGCCCCCTA
 TGTCAGAGCTGACAGAGACTGTGGTCTGTGCCCTGGGGTTGACCGTGGGCTTGTGGGTA
 TCGTGGTGGGCACCATCTTCATCATCCAAGGCCTGCGCTCAGGTGGGGCTCCAGACACC
 AGGGTCCCTTGTGAGTCGCACCCTAGAAAGGAAGGTGCTCTGCCGATCTATGAGAGCAGA
 AGAGTGGACGTGCTAGACGACCTAGAACTAGTTTCTGGCAAAGTTCATCATATACTCTCT
 CTTCCCTGATACTCTGCCCCCTCCTCTCTTCTCTGGGACTTAAGATGCTGTATCATTTTCAG
 AGCTCACATATACCTCAGAGTTCTCCCCTGACTTTCTGATATTTTTTTCTGTTCTCAGTA
 GTTGCCTACCATGAGATCACTGGGGTATTCCACCCTACTACTCACCCAGGTTGGAGTGAG
 TTACCTTACCACCCTAGTGACCTTGACCCCGTATTGCCATGGAAGCAATAAACTCCTCTT TAATAG

>ENA|D50047|D50047.1 Bos taurus BoLA-DQA2 mRNA for MHC class II DQA2,
 partial cds, clone: KQ217.

GCTCTAAAGCTGAACAGAGCTCTGATTCTAGGGGCCCTCGCCCTGACCACCATGATGAGC
 TCCAGTGGAGGTGAAGACATTGTGGCTGACCACGTTGGCTCCTATGGCACAGAGATCTAC
 CAATCTCATGGTCCCTCTGGCCAGTACACCCAGGAATTTGATGGAGACGAGATGTTTTAT
 GTGGACCTGGGGAAGAAGGAGACTGTCTGGAGGCTGCCTATGTTTAGCCAGTTTGCAGGT
 TTTGACCCACAGGCTGCACTGAGTGAAATAGCTACAGCAAAACACAACCTGGATGTCCTG
 ACTAAACGCTCCAACCTTTACCCCTGTTATCAATGAGGTTCCAGAGGTGACTGTGTTTTCC
 AAGTCTCCCGTGATGCTGGGTGAGCCCAACACCCCTCATCTGTACGTGGACAACATTTTT
 CCCCCTGTGATCAACATTACATGGCTGAAGAACGGGCATGCAGTCACAGAGGGTGTCTCT
 GAGACCAGCTTCTCCCTAAGGATGATCATTCTTTCTCAAGATTGGTTATCTCACCTTC
 CTCCCTTCTGATAATGACATTTATGACTGCAAAGTGGAGCACTGGGGTCTGGATGAGCCA
 CTTCTGAAACACTGGGGTATGTACGAGTTCCACCCTTTAGGTACTCTCTCTTTTTTCTAC
 CCAATACAAAACACTCTGAGTTTTTGGTCCCTCAATCTCACAGTCCAAAGCTTGTTTTCCA
 CACTTCAAGGTTTCTAAAATTATACTTCATTCTCTTCCTAAGCCTGGTGCCCTGAGTTTT
 TGTAGAATAAACACACACCTCCTGCCTAATCTCATGCACAGGCACACTCAGTATTCTGA
 CTTTCATAACTTCACTTTTCCAGAGCCAGAGGTTCCAGCCCCCTATGTCAGAGCTGACAGA
 GACTGTGGTCTGTGCCCTGGGGTTGACCGTGGGCTTGTGGGTATCGTGGTGGGCACCAT
 CTTTCATCATCCAAGGCCTGCGCTCAGGTGGGGCCTCCAGACACCAGGGTCCCTTGTGAGT
 CGCACCCCTAGAAAGGAAGGTAAGGATTTCATATTTGTCAGTGCCACAGACACACTTCAGGA
 GAAAGCGAAGCGGGAAGAAGTTGTAGACACAAACGTGGTTGAAAAGTGGGAGAATTGGGA
 ACCAGCATGACTGCGGCACAGAAGCTCCCTAGGACTCATCAGTCTCATGTCTTTTCTCTGT
 TGCAGGTGCTCTGCCGATCTATGAGAGCAGAAGAGTGAGCTGCTAGACGACCTAGAACT
 AGTTTCTGGCAAAGTTCATCATATACTCTCTCTTCCCTGATACTCTGCCCCCTCCTCTCTT
 CTCTGGGACTTAAGATGCTGTATCATTTTCAGAGCTCACATATACCTCAGAGTTCTCCCCCT
 GACTTTCTGATATTTTTTTCTGTTCTCAGTAGTTGCCTACCATGAGATCACTGGGGTATT
 CCACCCTACTACTCACCCAGGTTGGAGTGAGCTTTAGAGCACAATGGATCTCGAGGTCGA

>ENA|D50048|D50048.1 Bos taurus mRNA for MHC class II DQA2 (BoLA-DQA2),
 complete cds.

CTCAGAACAGCCACTGGTGAGTCCACCTTGAGAAGAGGATGGTCTGAAACAGAGCCCTGA
 TTCTAGGGGGCCCTCGCCCTGACCACCATGATGAGCTCCAGTGGAGGTGAAGACATTGTGG
 CTGACCACGTTGGCTCCTATGGCACAGAGATCTACCAATCTCATGGTCCCTCTGGCCAGT
 ACACCCAGGAATTTGATGGAGACGAGATGTTTTATGTGGACCTGGGGAAGAAGGAGACTG

TCTGGAGGCTGCCTATGTTTAGCCAGTTTGCAGGTTTTGACCCACAGGCTGCACTGAGTG
 AAATAGCTACAGCAAAACACAACCTTGGATGTCTGACTAAACGCTCCAACCTTTACCCCTG
 TTATCAATGAGGTTCCAGAGGTGACTGTGTTTTCCAAGTCTCCCGTGATGCTGGGTCAGC
 CCAACACCCCTCATCTGTCACGTGGACAACATTTTTCCCCCTGTGATCAACATTACATGGC
 TGAAGAACGGGCATGCAGTCACAGAGGGTGTTTCTGAGACCAGCTTCCTCCCTAAGGATG
 ATCATTCTTTTCTCAAGATTGGTTATCTCACCTTCCTCCCTTCTGATAATGACATTTATG
 ACTGCAAAGTGGAGCACTGGGGTCTGGATGAGCCACTTCTGAAACACTGGGGTATGTACG
 AGTTCCACCCCTTTAGGTACTCTCTCTTTTTCTACCCAATACAAAAACTCTGAGTTTTG
 GTCCCTCAATCTCACAGTCCAAAGCTTGTTTTCCACACTTCAAGGTTTCTAAAATTATAC
 TTCATTCTCTTCTAAGCCTGGTGCCCTGAGTTTTTGTAGAATAAACACCACACCTCCTG
 CCTAATCTCATGCACAGGCACACTCAGTATTCTG

>ENA|D50049|D50049.1 Bos taurus mRNA for MHC class II DQA2 (BoLA-DQA2), complete cds.

CTGAACAGAGCCCTGATTCTAGGGGCCCTCGCCCTGACCACCATGATGAGCTCCAGTGGA
 GGTGAAGACATTGTGGCTGACCACGTTGGCTCCTATGGCACAGAGATCTACCAATCTCAT
 GGTCCCTCTGGCCAGTACACCCAGGAATTTGATGGAGACGAGATGTTTTATGTGGACCTG
 GGGAAGAAGGAGACTGTCTGGAGGCTGCCTATGTTTAGCCAGTTTGCAGGTTTTGACCCA
 CAGGCTGCACTGAGTGAAATAGCTACAGCAAAACACAACCTTGGATGTCTGACTAAACGC
 TCCAACCTTTACCCCTGTTATCAATGAGGTTCCAGAGGTGACTGTGTTTTCCAAGTCTCCC
 GTGATGCTGGGTCAGCCCAACACCCCTCATCTGTCACGTGGACAACATTTTTCCCCCTGTG
 ATCAACATTACATGGCTGAAGAACGGGCATGCAGTCACAGAGGGTGTTTCTGAGACCAGC
 TTCCTCCCTAAGGATGATCATTCTTTTCTCAAGATTGGTTATCTCACCTTCCTCCCTTCT
 GATAATGACATTTATGACTGCAAAGTGGAGCACTGGGGTCTGGATGAGCCACTTCTGAAA
 CACTGGGGTATGTACGAGTTCCACCCCTTTAGGTACTCTCTCTTTTTCTACCCAATACAA
 AACACTCTGAGTTTTTGGTCCCTCAATCTCACAGTCCAAAGCTTGTTTTCCACACTTCAAG
 GTTTCTAAAATTATACTTCACTCTCTTCTAAGCCTGGTGCCCTGAGTTTTTGTAGAATA
 AACACCACACCTCCTGCCTAATCTCATGCACAGGCACACTCAGTATTCTGACTTTCATAA
 CTTCACTTTTCCAGAGCCAGAGGTTCCAGCCCTATGTCAGAGCTGACAGAGACTGTGGT
 CTGTGCCCTGGGGTTGACCGTGGGCCTTGTTGGGTATCGTGGTGGGCACCATCTTCATCAT
 CCAAGGCCTGCGCTCAGGTGGGGCCTCCAGACACCAGGGTCCCTTGTTGAGTCGCACCCTA
 GAAAGGAAGGTAAGGATTCATATTTGTCTAGTGCCACAGACACACTTCAGGAGAAAGCGAA
 GCGGGAAGAAGTTGTAGACACAAACGTGGTTGAAAAGTGGGAGAATTGGGAACCAGCATG
 ACTGCGGCACAGAAGCTCCCTAGGACTCATCAGTCTCATGTCTTTTCTGTTGACGGTGC
 TCTGCCGATCTATGAGAGCAGAAGAGTGGACGTGCTAGACGACCTAGAACTAGTTTCTGG
 CAAAGTTCATCATATACTCTCTCTTCCCTGATACTCTGCCCCCTCCTCTCTTCTCTGGGAC
 TTAAGATGCTGTATCATTTTCAGAGCTCACATATACCTCAGAGTTCTCCCTGACTTTCTG
 ATATTTTTTTCTGTTCTCAGTAGTTGCCTACCATGAGATCACTGGGGTATTCCACCCTAC
 TACTACCCAGGTTGGAGTGAGCTTTAGAGCACAAATGGATCTCGAGG

>ENA|U80857|U80857.1 Bos taurus MHC class II antigen (BoLA-DQA2) gene, allele 1db, partial cds.

GACCACGTTGGCACTTATGGCACAGACTTCTACCAATCTCATGGTCCTTCTGGCCAGTAC
 ATCCACCAATTTGATGGAGACGAGGAGTTTTATGTGGACCTGGAGAAGGAAGAGGCTGTC
 TGGAGGCTGCCTATGTTTGATAAATTACGTTTTCCACCCGCAAGGTGCACTGAGAAACATA
 GCTATAGCGAAACACAACCTTGGATGTTCTGACAAAGCTCTACAACCTTTACCCCTGTTATC AAT

>ENA|U80858|U80858.1 Bos taurus MHC class II antigen (BoLA-DQA2) gene, allele 5, partial cds.

GACCACGTTGGCACTTATGGCACAGACTTCTACCAATCTCATGGTCCTTCTGGCCAGTAC
 ATCCACCAATTTGATGGAGACGAGGAGTTTTATGTGGACCTGGAGAAGGAAGAGGCTGTC
 TGGAGGCTGCCTATGTTTGATAAATTACGTTTTCCACCCGCAAGGTGCACTGAGAAACATA
 GCTATAGCGAAACACAACCTTGGATGTTCTGACAAAACCTCTACAACCTTTACCCCTGTTATC AAT

>ENA|U80859|U80859.1 Bos taurus MHC class II antigen (BoLA-DQA2) gene, allele 14, partial cds.

GACCACGTTGGCACTTATGGCGCAGACTTCTACCAATCTCATGGTCCTTCTGGCCAGTAC
 ATCCACCAATTTGATGGAGACGAGGAGTTTTATGTGGACCTGGAGAAGGAAGAGGCTGTC
 TGGAGGCTGCCTATGTTTGATAAATTACGTTTTCCACCCGCAAGGTGCACTGAGAAACATA
 GCTATAGCGAAACACAACCTTGGATGTTCTGACAAAACCTCTACAACCTTTACCCCTGTTATC AAT

>ENA|U80860|U80860.1 Bos taurus MHC class II antigen (BoLA-DQA2) gene, allele 13, partial cds.
GACCACGTTGGCTCCTATGGCACAGACTTCTACCAATCTCATGGTCCCTCTGGCCAGTAC
ATCCATGAATTTGATGGAGATGAGTTGTTTTATGTGGACCTGGGGAAGAAGAGACTGTC
TGGCAGCTGCCTATGTTTGGTGAATTAACAAGTTTTGAAGCACAAAGATGCGTGAAATGAA
ATAGCTAAAGCAAAACACACCTTGGATGTCCTGACTAAACGCTCCAACCTTTACCCCTGTT ATCAAT

>ENA|U80861|U80861.1 Bos taurus MHC class II antigen (BoLA-DQA2) gene, allele 72, partial cds.
GACCACGTTGGCTCCTATGGCACAGAGATCTACCAATCTCATGGTCCCTCTGGCCAGTAC
ACCCAGGAATTTGATGGAGACGAGCTGTTTTATGTGGACCTGGGGAAGAAAGAGACTGTC
TGGAGGCTGCCTATGTTTAGCCAGTTTGCAGGGTTTGACCCACAGGCTGCACTGAGTGAA
ATAGCTACAGCAAAACACAACCTTGGATGTCCTGACTAAACGCTCCAACCTTTACCCCTGTT ATCAAT

>ENA|U80862|U80862.1 Bos taurus MHC class II antigen (BoLA-DQA2) gene, allele 73, partial cds.
GACCACGTTGGCTCCTATGGCACAGAGATCTACCAATCTCATGGTCCCTCTGGCCAGTAC
ACCCAGGAATTTGATGGAGACGAGATGTTTTATGTGGACCTGGGGAAGAAAGAGACTGTC
TGGAGGCTGCCTATGTTTAGCCAGTTTGCAGGGTTTGACCCACAGGCTGCACTGAGTGAA
ATAGCTACAGCAAAACACAACCTTGGATGTCCTGACTAAACGCTCCAACCTTTACCCCTGTT ATCAAT

>ENA|U80863|U80863.1 Bos taurus MHC class II antigen (BoLA-DQA2) gene, allele 11a2, partial cds.
GACCACGTTGGCTCCTATGGCACAGAGATCTACCAATCTCATGGTCCCTCTGGCCAGTAC
ACCCAGGAATTTGATGGAGACGAGATGTTTTATGTGGACCTGGGGAAGAAGGAGACTGTC
TGGAGGCTGCCTATGTTTAGCCAGTTTGCAGGGTTTGACCCACAGGCTGCACTGAGTGAA
ATAGCTACAGCAAAACACAACCTTGGATGTCCTGACTAAACGCTCCAACCTTTACCCCTGTT ATCAAT

>ENA|U80864|U80864.1 Bos taurus MHC class II antigen (BoLA-DQA2) gene, allele 11c, partial cds.
GACCACGTTGGCTCCTATGGCACAGAGATCTACCAATCTCATGGTCCCTCTGGCCAGTAC
ACCCAGGAATTTGATGGAGACGAGATGTTTTATGTGGACCTGGGGAAGAAGGAGACTGTC
TGGAGGCTGCCTATGTTTAGCCAGTTTGCAGGGTTTGACCCACAGGCTGCACTGAGTGAA
ATAGCTACATCAAAACACAACCTTGGATGTCCTGACTAAACGCTCCAACCTTTACCCCTGTT ATCAAT

>ENA|U80865|U80865.1 Bos taurus MHC class II antigen (BoLA-DQA2) gene, allele 11a1, partial cds.
GACCACGTTGGCTCCTATGGCACAGAGATCTACCAATCTCATGGTCCCTCTGGCCAGTAC
ACCCAGGAATTTGATGGAGACGAGATGTTTTATGTGGACCTGGGGAAGAAGGAGACTGTC
TGGAGGCTGCTTATGTTTAGCCAGTTTGCAGGGTTTGACCCACAGGCTGCACTGAGTGAA
ATAGCTACAGCAAAACACAACCTTGGATGTCCTGACTAAACGCTCCAACCTTTACCCCTGTT ATCAAT

>ENA|U80866|U80866.1 Bos taurus MHC class II antigen (BoLA-DQA2) gene, allele 11b, partial cds.
GACCACGTTGGCTCCTATGGCACAGAGATCTACCAATCTCATGGTCCCTCTGGCCAGTAC
ACCCAGGAATTTGATGGAGACGAGATGTTTTATGTGGACCTGGGGAAGAAGGAGACTGTC
TGGAGGCTGCCTACGTTTAGCCAGTTTGCAGGGTTTGACCCACAGGCTGCACTGAGTGAA
ATAGCTACATCAAAACACAACCTTGGATGTCCTGACTAAACGCTCCAACCTTTACCCCTGTT ATCAAT

>ENA|U80867|U80867.1 Bos taurus MHC class II antigen (BoLA-DQA2) gene, allele 1db, partial cds.
GACCACGTTGGCTCCTATGGCACAGAGATCTACCAATCTCATGGTCCCTCTGGCCAGTAC
ACCCAGGAATTTGATGGAGACGAGATGTTTTATGTGGACCTGGGGAAGAAGGAGACTGTC
TGGAGGCTGCCTATTTTTAGCCAGTTTGCAGGGTTTGACCCACAGTTTGCCTGAGTGAA
ATAGCTACATCAAAACACAACCTTGGATGTCCTGACTAAACGCTCCAACCTTTACCCCTGTT ATCAAT

>ENA|U80868|U80868.1 Bos taurus MHC class II antigen (BoLA-DQA2) gene, allele 6, partial cds.
GACCACGTTGGCTCCTATGGCACAGAGATCTACCAATCTCATGGTCCCTCTGGCCAGTAC
ACCCACGAATTTGATGGAGACGAGCTGTTTTATGTGGACCTGGGGAAGAAGGAGACTGTC
TGGAGGCTGCCTATGTTTGGTGATTTAACAAGTTTTGACCCACAGGGTGCCTGAGTGAA
ATAGCTACATCAAAACACAATTTGGATATCCTGACTAGACGCTCCAACCTTTACCCCTGCC ATCAAC

>ENA|Y14020|Y14020.1 Bos indicus BoLA DQA3 gene
 GTCCTAAACAGAGCTCTGATTCTGGGGGCCCTCACCTGACCACCATGACAAGCCTCTGT
 GGAGGTGAAGACATTGTGGCGGACCACGTTGGCACTTATGGCAGAGACTTCTACCAATCT
 CATGGTCCCTTCTGGCCAGTACATCCACCAATTTGATGGAGACGAGGAGTTTATGTGGAC
 CTGGAGAAGGAAGAGGCTGTCTGGAGGCTGCCTATGTTTGATAAAATTACGTTTTCACCCG
 CAAGGTGCACTGAGAAACATAGCTATAGCGAAACACAACCTTGGATGTTCTGACAAAACCTC
 TACAACCTTTACCCCTGTTATCAATGAGGTTCCAGAGGTGACTGTGTTTTCCAGTCTCCC
 GTGATGCTGAGTCAGCCCAATACCCTCATCTGTACGTGGACAACATCTTTCCCCCTGTG
 ATCAACATCACATGGTTGAGAAACGGGCACTCTGTACAGAGCATGTTTCTGAGACCAGC
 TTCCTCCTCAGAAGTGATTATTCCTACCTCAAGATAAGTTATCTCCCCTTCCGCCCTTCT
 GATGATGATGTTTATGACTGCAAAGTGAGCACTGGGGCCTGGATGAGCCACTGCTCAAA
 CACTGGGAGCCTGAAATTCCAGCCCCCTATGTCAGAGCTGACAGAGACTGTGGTCTGTGCC
 CTGGGGTTGACCGTGGGCCTCGTGGGCATCGTGGTGGGCACTGTCTCATCACCCGAGGT
 CTGCGCTCAAGTGGGGCCTCCAGACACCAAGGGCCCTTGTGAGTCACACTCCAGTAGGAA
 GGTGTACTGTCCATCTACAAGAACAGAAAAATGGACATACTAGATGACCTGGAACATTTT
 TCTGGCCAAGTTCATCACGTACCTTTTCTCCTTCTGCCCTCCTCT

>ENA|Y14021|Y14021.1 Bos indicus BoLA DQA3 gene, isolate E223
 GTCCTAAACAGAGCTCTGATTCTGGGGGCCCTCACCTGACCACCATGACAAGCCTCTGT
 GGAGGTGAAGACATTGTGGCGGACCACATTGGCACTTATGGCAGAGACTTCTACCAATCT
 CATGGTCCCTTCTGGCCAGTACATCCACCAATTTGATGGAGACGAGGAGTTTATGTGGAC
 CTGGAGAAGGAAGAGGCTGTCTGGAGGCTGCCTATGTTTGATAAAATTAAGACGTTTTTAC
 CCGCAAGGTGCACTGAGAAACATAGCTGTAGCGAAACACAACCTTGGATGTCTGACTAAA
 CGCTACAACCTTTACCCCTGTTATCAATGAGGTTCCAGAGGTGACTGTGTTTTCCAGTCT
 CCCGTGATGCTGAGTCAGCCCAATACCCTCATCTGTACGTGGACAACATCTTTCCCCCT
 GTGATCAACATCACATGGTTGAGAAACGGGCACTCTGTACAGAGCATGTTTCTGAGACC
 AGCTTCCTCCTCAGAAGTGATTATTCCTACCTCAAGATAAGTTATCTCCCCTTCCACCCT
 TCTGATGATGATGTTTATGACTGCAAAGTGAGCACTGGGGCCTGGATGAGCCACTGCTC
 AAACACTGGGAGCCTGAAATTCCAGCCCCCTATGTCAGAGCTGACAGAGACTGTGGTCTGT
 GCCCTGGGGTTGACAGTGGGCCTCGTGGGCATCGTGGTGGGCACTGTCTCATCACCCGA
 GGTCTGCGCTCAAGTGGGGCCTCCAGACACCAAGGGCCCTTGTGAGTCACACTCCAGTAG
 GAAGGTGTACTGTCCATCTACAAGAACAGAAAAATGGACATACTAGATGACCTGGAACATA
 TTTTCTGGCCAAGTTCATCACGTACCTTTTCTCCTTCTGCCCTCCTCT

>ENA|Y14022|Y14022.1 Bos indicus BoLA DQA3 gene, isolate F100
 GTCCTAAACAGAGCTCTGATTCTGGGGGCCCTCACCTGACCACCATGACAAGCCTCTGT
 GGAGGTGAAGACATTGTGGCTGACCACATTGGCACCTACGGCGCAGACTTCTACCAATCT
 CATGGTCCCTTCTGGCCAGTACATCCACGAATTTGATGGAGACGAGTTGTTTTATGTGGAC
 CTGGGGAAGAAGGAGACTGTCTGGCAGCTGCCTATGTTTGTTGTAATTAACAAGTTTTGAA
 GCACAAGATGCGCTGAATGAAATAGCTAAAGCAAAACACACCTTGGATGTCTGACTAAA
 CGCTCCAACCTTTACCCCTGTTATCAATGAGGTTCCCTGAGGTGACTGTGTTTTCCAGTCT
 CCCATGATGCTGGGTGAGCCCAACACCCTCATCTGCCACGTGGACAACATTTTTCCCCCT
 GTGATCAACATCACATGGTTGAGGAATGGGCATGCAGTCACAGAGGGTGTCTCTGAGACC
 AGCTTCCTCCCCAAAAGTGATTATTCCTTCCTCAAGATTGGTTATCTTACCTTCCTCCCT
 TCTGATGATGATGTTTACGACTGCAAAGTGAGCACTGGGGCCTGGATGAGCCACTTCTG
 AAACACTGGGAGCCTGAGATTCCAGCCCCCTATGTCAGAGCTGACAGAGACTGTGGTCTGT
 GCCCTGGGGTTGACTGTGGGCCTCGTGGGCATCGTGGTGGGCACTGTCTCATCATCCGA
 GGTCTGCGCTCAGGTGGAGCCTCCAGACACCAAGGGTCCCTTGTGAGTCACACTCCAGTAG
 GAAGGTGCACTGTCCATCTACAAGAACAGAAAAATGGACATACTAGATGACCTGGAACATA
 TTTTCTGGCCAAGTTCATCATGTACCTTTTCTCCTTCTGCCCTCCTCT

>ENA|Z48185|Z48185.1 B.taurus BoLA-DQA gene (exon 2) for first domain of
 MHC class 2 molecule, alpha chain.
 GCGCCTATGGCATAAACGTCTACCAACATATGGTCCCTCTGGCTACTATACCCATGAAT
 TTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTCTGGCGTCTGC
 CTGTGTTTAGTAAATTTACAAGTTTTGACCCTCAGGGTGCGCTGAGAAACATAGCTACAG
 CGAAGCACAAATTTGGAGGTCTTGATTCAAAGGTCCAACCTCTACTGCTG

>ENA|Z48186|Z48186.1 B.taurus BoLA-DQA gene for first domain of MHC class
 2 molecule, alpha chain.
 GCGCCTATGGCATAAACGTCTACCACTCATATGGTCCCTCTGGCTACTATACCCATGAAT
 TTGATGGAGATGAACAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTCTGGCGTCTGC

CTGTGTTTAGTAAATTTGCAAGTTTTGACCCTCAGGGTGCGCTGAGAAACATAGCTACAG
CGAAGCACAATTTGGAGATTATGATTCAAGAGTCCAACCTCTACTGCTG

>ENA|Z48187|Z48187.1 B.taurus, B.indicus BoLA-DQA gene for first domain
of MHC class 2 molecule, alpha chain.

GTGCCTATGGCATAAACGTCTACCACACATATGGTCCCTCTGGCTACTATACCCATGAAT
TTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTCTGGCGTCTGC
CTGTGTTTAGTAAATTTACAAGTTTTGACCCTCAGGGTGCGCTGAGAAACATAGCTACGA
CGAAGCACAATTTGGAGATCATGATTCAAGGTCCAACCTCTACTGCTG

>ENA|Z48188|Z48188.1 B.taurus, B.indicus BoLA-DQA gene for first domain
of MHC class 2 molecule, alpha chain.

GTGCCTATGGCATAAACATCTACCACACATATGGTCCCTCTGGCTACTATACCCATGAAT
TTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTCTGGAACTCTGC
CTCTGTTTAGTAAATTTAGACGTTTTGACCCTCAGGGTGCGCTGAGAAACATAGCTACAG
CGAAGCACAATTTGGAGATCGTGATTCAAAGGTCCAACCTCTACTGCTG

>ENA|Z48189|Z48189.1 B.taurus, B.indicus BoLA-DQA gene for first domain
of MHC class 2 molecule, alpha chain.

GCGCCTATGGCATAAACGTCTACCACTCATATGGTCCCTCTGGCTACTATACCCATGAAT
TTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTCTGGCGTCTGC
CTGTGTTTAGTAAATTTGCAAGTTTTGACCCTCAGGGTGCGCTGAGAAACATAGCTGTGG
GGAAACGGACTTTGGAGGTCATGATTCAAGGTCCAACCTCTACTGCTG

>ENA|Z48190|Z48190.1 B.indicus BoLA-DQA gene for first domain of MHC
class 2 molecule, alpha chain.

GCGCCTATGGCATAAACGTCTACCACACATATGGTCCCTCTGGCTACTTTACCCATGAAT
TTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTCTGGAATCTGC
CTCTGTTTAGTAAATTTAGACGTTTTGACCCTCAGGGTGCGCTGAGAAACATAGCTACAG
TGAAGCACAATTTGGAGATCGTGATTCAAAGGTCCAACCTCTACTGCTG

>ENA|Z48191|Z48191.1 B.indicus, B.taurus BoLA-DQA gene for first domain
of MHC class 2 molecule, alpha chain.

GCACCTATGGCATAAGCATCTACCACACATATGGTCCCTCTGGCTACTATACCCATGAAT
TTGATGGAGATGAAGAGTTCTACGTGGACCTAGAAAAGAGGGAGACTGTCTGGCGTCTGC
CTGTGTTTAGTAAATTTACAAGTTTTGACCCTCAGGGTGCGCTGAGAAACATAGCTATAG
TGAAGCACAATTTGGAGATCGTGATTCAAAGGTCCAACCTCTACTGCTG

>ENA|Z48192|Z48192.1 B.indicus, B.taurus BoLA-DQA gene for first domain
of MHC class 2 molecule, alpha chain.

GCGCCTATGGCATAAACGTCTACCACTCATATGGTCCCTCTGGCTACTATACCCATGAAT
TTGATGGAGATGAACAGTTCTACGTGGACCTGGAAAAGAAGGAGACTGTCTGGCGTCTGC
CTGTGTTTAGTAAATTTGCAACTTTTGACCCTCAGGGTGCGCTGAGAAACATAGCTGTGG
GGAAACAGACTTTGGAGGTCATGATTCAAGGTCCAACCTCTACTGCTG

>ENA|Z48193|Z48193.1 B.taurus BoLA-DQA gene for first domain of MHC class
2 molecule, alpha chain.

GCACCTATGGCATAAGCATCTACCACACATATGGTCCCTCTGGCTACTATACCCATGAAT
TTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTCTGGCGTCTGC
CTGTGTTTAGTAAATTTGCAACTTTTGACCCTCAGGGTGCGCTGAGAAACATAGCTACGA
CGAAGCACAATTTGGAGATCGTGATTCAAAGGTCCAACCTCTACTGCTG

>ENA|Z48194|Z48194.1 B.taurus BoLA-DQA gene for first domain of MHC class
2 molecule, alpha chain.

GCGCCTATGGCATAAACGTCTACCACACATATGGTCCCTCTGGCTACTATACCCATGAAT
TTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTCTGGCGTCTGC
CTGTGTTTAGTAAATTTACAAGTTTTGACCCTCAGGGTGCGCTGAGAAACATAGCTACAG
TGAAGCACAATTTGGAGATCTTGATTCAAAGGTCCAACCTCTACTGCTG

>ENA|Z48195|Z48195.1 B.indicus BoLA-DQA gene for first domain of MHC
class 2 molecule, alpha chain.

GCGCCTATGGCATAAACGTCTACCACTCATATGGTCCCTCTGGCTACTATACCCATGAAT
TTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAGAGGGAGACTGTCTGGAATCTGC

CTCTGTTTAGTAAATTTAGACGTTTTGACCCTCAGGGTGCGCTGAGAAACATAGCTACGA
CGAAGCACAATTTGGAGATCATGATGCAAAGGTCCAACCTCTACTGCTG

>ENA|Z48196|Z48196.1 B.indicus BoLA-DQA gene for first domain of MHC
class 2 molecule, alpha chain.

GCGCCTATGGCATAAACGTCTACCACTCATATGGTCCCTCTGGCTACTATACCCATGAAT
TTGATGGAGATGAAGAGTTCTACGTGGACCTGGAAAAAGAGGGAGACTGTCTGGAACTCTGC
CTCTGTTTAGTAAATTTAGACGTTTTGACCCTCAGGGTGCGCTGAGAAACATAGCTACAG
CGAAGCACAATTTGGAGGTCTTGATTCAAAGGTCCAACCTCTACTACTG

>ENA|Z48197|Z48197.1 B.taurus BoLA-DQA gene for first domain of MHC class
2 molecule, alpha chain.

GCATCTATGGCATAAGCATATATCAGTCTTATGGTCCCTCTGGCCAGTACACCCATGAAT
TTGATGGAGATGAGCAGTTCTATGTGGACCTGGAGAAGAAGGAGACTGCCTGGCAGCTGC
CCCTATTTAGCAGAATGTTAAGTTTTGACCCACAGTTAGCACTGAGAAACATAGCTATCA
TGAAACTTCATGTGGACTTCCTGACTAAATTCTCCAACCTCTACTGCTG

Goat

>ENA|AY829349|AY829349.1 Capra hircus MHC class II antigen (Cahi-DQA2)
gene, Cahi-DQA2*0101 allele, exon 2 and partial cds.

CTTCCTGCTCCTCACCCCTCACAGCTGACCACGTTGGCATCTATGGCGCAGACCTCTACCA
ATCTCATGGTCCCTCTGGCCAGTACACCCACGAATTTGATGGGGACGAGCTGTTTTATGT
GGACCTGGGGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGGTGAATTCACAAGTTT
TGACCCGCAAGGTGCACTGAGTGAAATAGCTAAAGCAAAACACAACCTGGATATCATGAT
TAAACGTTCCAACCTTTACCCCTGTTATCAATGGTAAGTGTCCACCATTCTACTTCTTT

>ENA|AY829350|AY829350.1 Capra hircus MHC class II antigen (Cahi-DQA2)
gene, Cahi-DQA2*0102 allele, exon 2 and partial cds.

CTTCCTGCTCCTCACCCCTCACAGCTGACCACGTTGGCATCTATGGCGCAGACCTCTACCA
ATCTCATGGTCCCTCTGGCCAGTACACCCACGAATTTGATGGGGACGAGCTGTTTTATGT
GGACCTGGGGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGGTGAATTAACAAGTTT
TGACCCGCAAGGTGCACTGAGTGAAATAGCTAAAGCAAAACACAACCTGGATATCATGAT
TAAACGTTCCAACCTTTACCCCTGTTATCAATGGTAAGTGTCCACCATTCTACTTCTTT

>ENA|AY829351|AY829351.1 Capra hircus MHC class II antigen (Cahi-DQA2)
gene, Cahi-DQA2*0201 allele, exon 2 and partial cds.

CTTCCTGCTCCTCACCCCTCACTTACAGCTGACCACGTTGGCTCCTACGGCACAGACTTCT
ACCAATCTCATGGTCCCTCTGGCCAGTTACCCAGGAATTTGATGGAGACGAGTTGCTTT
ATGTGGACCTGGGGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTAGCCAGTTTGCAG
GTTTTGACCCTCAAGGTGCACTGAGGAACATAGCTACAGCAAAAGACACCTTGATATCC
TGACTAAACGCTCCAACCTCTACCCAGTTATCAATGGTAAGTGTCCACCATTCTACTTCT
CTTT

>ENA|AY829352|AY829352.1 Capra hircus MHC class II antigen (Cahi-DQA2)
gene, Cahi-DQA2*03011 allele, exon 2 and partial cds.

CTTCCTGCTCCTCACCCCTCACTTACAGCTGACCACGTTGGCTCCTATGGCACAGAGATCT
ACCAATCTCATGGTCCCTCTGGCCAGTACACCCAGGAATTTGATGGAGACGAGATGTTTT
ATGTGGACCTGGGGAAGAAGGAGACTGTCTGGAGACTGCCTATGTTTAGCCAGTTTGCAG
GTTTTGATCCACAGGGTGCCTGAGTGAAATAGCTACAGCAAAACAAAACCTTGATATCC
TGACTAAACACTCCAACCTTTACCCCTGCTATCAATGGTAAGTGTCCACCATTCTACTTCT
CTTT

>ENA|AY829353|AY829353.1 Capra hircus MHC class II antigen (Cahi-DQA2)
gene, Cahi-DQA2*03012 allele, exon 2 and partial cds.

CTTCCTGCTCCTCACCCCTCACTTACAGCTGACCACGTTGGCTCCTATGGCACAGAGATCT
ACCAATCTCATGGTCCCTCTGGCCAGTACACCCAGGAATTTGATGGAGACGAGATGTTTT
ATGTGGACCTGGGGAAGAAGGAGACTGTCTGGAGACTGCCTATGTTTAGCCAGTTTGCAG
GTTTTGATCCACAGGGTGCCTGAGTGAAATAGCTACGGCAAAACAAAACCTTGATATCC
TGACTAAACACTCCAACCTTTACCCCTGCTATCAATGGTAAGTGTCCACCATTCTACTTCT
CTTT

>ENA|AY829354|AY829354.1 Capra hircus MHC class II antigen (Cahi-DQA2) gene, Cahi-DQA2*0401 allele, exon 2 and partial cds.
CTTCCTGCTCCTCACCTCACTTACAGCTGACCACGTTGGCTCCTATGGCACAGTTATCT
ACCAATCTCATGGTCCCTCTGGCCAGTTCACCCAGGAATTTGATAGAGACGAGCTGTTTT
ATGTGGACCTGGAGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTAGCCAGTTTGCA
GTTTTGACCCTCAAGGTGCACTGAGTAACATAGCTACAGCGAAACACAACCTTGATATCA
TGACTAAATTGCACAACCTTTACCCAGTTATCAACGGTAAGTGTCCACCATTCTACTTCT
CTTT

>ENA|AY829355|AY829355.1 Capra hircus MHC class II antigen (Cahi-DQA2) gene, Cahi-DQA2*0501 allele, exon 2 and partial cds.
CTTCCTGCTCCTCACCTCACTTATCAGCTGACCACGTTGGCTCCTACAGCACAGACTTC
TACCAATCTCATGGTCCCTCTGGCCAGTACACCCAGGAATTTGATGGAGACGAGATGTTT
TATGTGGACCTGGAGAAGAAGGAGACTGTCTGGAGGCTGCCTATGTTTAGCCAGTTTGCA
GGTTTTGACCCTCAAGGTGCACTGAGTAACATAGCTACAGCAAAACACAACCTTGATGTC
ATGACTAAATGGTACAACCTTTACCCAGTTATCAACAGTAAGTGTCCACCATTCTACTTC
TCTTT

>ENA|AY829356|AY829356.1 Capra hircus MHC class II antigen (Cahi-DQA2) gene, Cahi-DQA2*0601 allele, exon 2 and partial cds.
CTTCCTGCTCCTCACCTCACTTATCAGCTGACCACATTGGCTCCTATGGCACAACTATC
TACCAATCTCATGGTCCCTCTAGCCAGTACACCCAGGAATTTGATGGAGACGAACCTGTTT
TATGTGGACCTGGAGAAGAAGGAGACCGTCTGGCGGCTGCCTATGTTTAGCCAGTTTGCA
GGTTTTAACATTCAAGATGCACTGAATAACATACCTGCAGCGAAACACAACCTTGATATC
CTGACTAAACGCTCCAACCTTTACCCAGTTATCAACGGTAAGTGTCCACCATTCTACTTC
TCTTT

>ENA|AY829357|AY829357.1 Capra hircus MHC class II antigen (Cahi-DQA2) gene, Cahi-DQA2*0701 allele, exon 2 and partial cds.
CTTCCTGCTCCTCACCTCACTTATCAGCTGACCACATTGGCACCTATGGCACAGACTTC
TACCAATCTCATGGTCCCTCTAGTGAGTACACCCAGGAATTTGACGAAGACGAGCTGCTT
TATGTGGACCTGGAGAAGAAAGAGACTGTCTGGTGGCTGCCTATGTTTGGCCGGTTTGCA
GGTTTTACATTCAAGTTGCACTGAGTAACATAGCTACAGCGAAACACAACCTTGATGTC
ATGACTAAATGGTACAACCTTTACCCAGTTATCAACGGTAAGTGTCCACCATTCTACTTC
TCTTT

>ENA|AY829358|AY829358.1 Capra hircus MHC class II antigen (Cahi-DQA2) gene, Cahi-DQA2*0801 allele, exon 2 and partial cds.
CTTCCTGCTCCTCACCTCACTTATCAGCTGACCACATTGGCACCTATGGCGCAGACTTC
TACCAATCTCATGGTCCCTCTGGCCAGTACATCCACGAATTTGATGGAGACGAGCTGTTT
TATGTGGACCTGGGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGGTGAATTGACA
AGTTTTGACCCGCAAGGTGCACTAAATAACATAGCTATAGCGAAACACAACCTTGATAGT
CTGACTAAACTCTACAACCTTTACCCAGTTATCAACGGTAAGTGTCCACCATTCTACTTC
TCTTT

>ENA|AY829359|AY829359.1 Capra hircus MHC class II antigen (Cahi-DQA2) gene, Cahi-DQA2*0901 allele, exon 2 and partial cds.
CTTCCTGCTCCTCACCTCACTTATCAGCTGACCACGTTGGCATCTACGGCACAGACTTC
TACCAATCTCATGGTCCCTCTGGCGAGTACATCCACTTATTTGATGGAGACGAAGAGTTT
TATGTGGACCTGGAGAAGAAGGAGACTGTCTGGCGGCTGCCTATGTTTGAATTAAGA
AGATTTGACCCGCAAGGTGCACTAAATAACATAGCTATAGCGAAACACAACCTTGATATC
CTGACTAAACGCTACAACCTTTACCCAGTTATCAACGGTAAGTGTCCACCATTCTACTTC
TCTTT

4.4 DQB

Sheep

>ENA|AJ238931|AJ238931.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*13 allele, exon 2
GATTTTCGTGGTCCAGTTTAAGGGCTGTGTTACTTACCAACGGGACGGAGCGGGTGCGG
AGTGTGAACAGATACATCTACAACCAGGAGGAGTTCGTGCGCTTCGACAGCGACTGGGAC
GAGTACCGGGCGGTGACCCGCTGGGGCGGCGGAGCGCCGAGTACTGGAACAGCCAGAAG
GACATCATGGAGCAGACGCGGGCCGAGGCGGACACGGTGTGCAGACACAACCTACCAGAAC
GAGCTCATCACCTCCTTGCA

>ENA|AJ238932|AJ238932.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*14 allele, exon 2
GATTTTCGTGTACCAGTTTAAAGGGCCTGTGTTACTTCACCAACGGGACGGAGCGGGTGCGG
CTCGTGACCAGATACATCTACAACCAGGAGGAGTACGTGCGCTTCGACAGCGACTGGGAC
GAGTACCGGGCGGTGACCCGCTGGGGCGGGCGGAGCGCCGAGTACTGGAACAGCCAGAAG
GACATCCTGGAGCAGACGCGGGCCGCGGTGGACACGGTGTGCAGACACAACCTACCAGAAC
GAACTCATCACCTCCTTGCGAG

>ENA|AJ238933|AJ238933.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*15 allele, exon 2
GATTTTCGTGGTCCAGTTTAAAGGGCCTGTGTTACTTCACCAACGGGACGGAGCGGGTGCGG
CATGTGACCAGATACATCTACAACCAGGAGGAGTACGCGCGCTTCGACAGCGACTGGGAC
GAGTACCGGGCGGTGACCCGCTGGGGCGGGCGGACGCCGAGTACTGGAACAGCCAGGAG
GACATCCTGGAGCAGACGCGGGCCGAGGCGGACACGGTGTGCAGACACAACCTACCAGAAC
GAACTCATCACCTCCTTGCGAG

>ENA|AJ238934|AJ238934.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*16 allele, exon 2
GATTTTCGTGTTCCAGTTTAAAGGGCCTGTGTTACTTCACCAACGGGACGGAGCGGGTGCGG
AGTGTGAACAGATACATCTACAACCAGGAAGAGCACCTGCGCTTCGACAGCGACTGGGAC
GAGTACCGGGCGGTGACCCGCTGGGGCGGGCGGCACGCCGAGTACTTCAACAGCCAGAAG
GACTTCCTGGAGCGGACGCGGGCCGAGGCGGACACGGTGTGCAGAAACAACCTACCAGAAC
GAGCTCATCACCTCCTTGCGAG

>ENA|AJ238935|AJ238935.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*17 allele, exon 2
GATTTTCGTGGTCCAGTTTAAAGGGCCTGTGTTACTTCACCAACGGGACGGAGCGGGTGCGG
TACGTGACCAGATACATCTACAACCAGGAGGAGTACGTGCGCTTCGACAGCGACTGGGAC
GAGTACCGGGCGGTGACCCGCTGGGGCGGGCGGAAGCCGAGTACTGGAACAGCCAGAAG
GACATCATGGAGCAGACGCGGGCCGAGGTGGACACGGTGTGCAGAAACAACCTACCAGGCG
GAGCTCATCACCTCCTTGCGAG

>ENA|AJ238936|AJ238936.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*18 allele, exon 2
GATTTTCGTGTTCCAGTTTAAAGGGCCTGTGTTACTTCACCAACGGGACGGAGCGGGTGCGG
CTCGTGACCAGATACTTCTACAACCAGGAGGAGTACGCGCGCTTCGACAGCGACTGGGGC
GAGTACCGGGCGGTGACCCGCTGGGGCGGGCGGACGCCGAGTACTGGAACAGCCAGAAG
GACATCCTGGAGCGGGTGCGGGCCGAGGTGGACACGGTGTGCAGACACAACCTACCAGGTG
GATGCCCCCTTCACCTGGCAG

>ENA|AJ238937|AJ238937.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*19 allele, exon 2
GATTTTCGTGTACCAGTTTATATGCCACTGTTACTTCACCAACGGGACGGAGCGGGTGCGG
TACGTGACCAGATACATCTACAACCAGGAAGAGTTCGTGCGCTTCGACAGCGACTGGGAC
GAGCACCGGGCGGTGACCCGCTGGGGCGGGCGGACGCCGAGTACTGGAACAGCCAGAAG
GACATCCTGGAGCGGGTGCGGGCCGAGGTGGACACGGTGTGCAGAAACAACCTACCAGGGG
GAGCTCATCACCTCCTTGCGAG

>ENA|AJ238938|AJ238938.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*20 allele, exon 2
GATTTTCGTGCACCAGTTTAAAGGGCCTGTGTTACTTCACCAACGGGACGGAGCGGGTGCGG
AGTGTGAACAGATACATCTACAACCAGGAGGAGTACGTGCGCTTCGACAGCGACTGGGAC
GAGTACCGGGCGGTGACCCGCTGGGGCGGGCGGACGCCGAGTACTGGAACAGCCAGAAG
GACATCCTGGAGCGGGTGCGGGCCGAGGCGGACACGGTGTGCAGACACAACCTACCAGGTG
CATGCCCCCTTCACCTGGCAG

>ENA|AJ238939|AJ238939.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*21 allele, exon 2
GATTTTCGTGGTCCAGTTTAAAGGGCCTGTGTTACTTCACCAACGGGACGGAGCGGGTGCGG
CTCGTGACCAGATACTTATAACAACCAGGAGGAGTACGCGCGCTTCGACAGCGACTGGGGC
GAGTACCGGGCGGTGACCCGCTGGGGCGGGCGGAGCGCCGAGTACTGGAACAGCCAGAAG
GACATCCTGGAGCGGGTGCGGGCCGAGGCGGACACGGTGTGCAGACACAACCTACCAGGTG
TATGCCCCCTTCACCTGGCAG

>ENA|AJ238940|AJ238940.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*22 allele, exon 2
GATTTTCGTGTACCAGTTTAAGCCCTCCTGTACTTTCACCAACGGGACGGAGCGGGTGCGG
CTCGTGACCAGATACTTACACAACCGGGAGGAGTTCGTGCGCTTCGACAGCGACTGGGGC
GAGTACCGCGGGGTGACGCCGCCGGGGCAGCGGCAAGCCGAGTACTGGAACAGCCAGAAG
GACATCCTGGAGCAGACGCGGGCCGAGGTGGACACGGTGTGCAGACACAACCTACCAGGCG
GAGCTCATCACCTCCTTGCGAG

>ENA|AJ238941|AJ238941.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*23 allele, exon 2
GATTTTCGTGTTTCTGTTTATGGGCCAGTGTTACTTTCACCAACGGGACGGAGCGGGTGCGG
CTCGTGACCAGATACATCTACAACCGAGGAGTACGTGCGCTTCGACAGCGACTGGGGC
GAGTACCGGGCGGTGACGCCGCCGGGGCAGCGGCAAGCCGAGTACTTCAACAGCCAGAAG
GACTTCCTGGAGCAGACGCGGGCCGAGGCGGACACGGTGTGCAGACACAACCTACCAGGTG
GAAGCCGCCTTCACCTGGCAG

>ENA|AJ238942|AJ238942.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*24 allele, exon 2
GATTTTCGTGTTCAGTTTAAAGTGCCACTGTTACTTTCACCAACGGGACGGAGCGGGTGCGG
TACGTGACCAGATACATCTACAACCGGGAGGAGTACGCGCGCTTCGACAGCGACTGGGGC
GAGTACCGGGCGGTGACGCCGCCGGGGCAGCGGCAAGCCGAGTACTGGAACAGCCAGAAG
GACATCATGGAGCGGGTGCGGGCCGAGGTGGACACGGTGTGCAGAAACAACCTACCGGGTG
TATGCCCCCTTCACCTGGCAG

>ENA|AJ238943|AJ238943.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*25 allele, exon 2
GATTTTCGTGTATCAGTTTATAGGCCAGTGTTACTTTCACCAATGGGACAGAGCGGGTGCGG
CTTGTGAAAAGACAGATCTACAACCGGCAGGAGCACGTGCGATTTCGACAGCAACGTGAAC
GAGTTCCGGGCGGTTTCCCCGCTGGGGCGGCAGGATGCCGAGTACTTCAACAGCCACGAC
TTCCTGGAGCAGACGCGGGCCGAGGTGGACACGGTGTGCAGACACAACCTACCAACTGGAG
CTCATCACCTCCTTGCGAG

>ENA|AJ238944|AJ238944.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*26 allele, exon 2
GATTTTCGTGGTCCAGTTTATGGGCCTGTGTTACTTTCACCAACGGGACGGAGCGGGTGCGG
AGTGTGAACAGATACATCTACAACCGGGAGGAGTACGTGCGCTACGACAGCGACTGGGGC
GAGTACCGGGCGGTGACCCCGCTGGGGCTGCCGGACGCCGAGTACTGGAACAGCCAGGAG
GGCGAACTGGAGCGGGTGCGGGCAGAGACAGACACGGTGTGCAAACACAACCTACCAACTG
GAGCTCATCACCTCCTTGCGAG

>ENA|AJ238945|AJ238945.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*27 allele, exon 2
GATTTTCGTGCACCAGTTTAAGGGCCGGTGTTACTTTCACCAACGGGACGGAGCGGGTGCGG
CATGTGACCAGATACATCTACAACCGGGAGGAGTACGCGCGCTTCGACAGCGACTGGGAC
GAGTACCGGGCGGTGACGCCGCTGGGGCGGCGGAGCGCCGAGTACTGGAACAGCCAGGAG
GACATCCTGGAGCAGACGCGGGCCGAGGTGGACAGGGTGTGCAGACACAACCTACCGGGTG
TATGCCCCCTTCACCTGGCAG

>ENA|AJ238946|AJ238946.1 Ovis aries Ovar-DQB gene for MHC class II antigen, DQB*28 allele, exon 2
GATTTTCGTGTACCAGTTTAAGGGCCTGTGTTACTTTCACCAACGGGACGGAGCGGGTGCGG
CTCGTGACCAGATACTTCTACAACCGGCAGGAGGACGTGCGCTTCGACAGCGACTGGGGC
GAGTACCGGGCGGTGACGCCGCTGGGGCGGCGGCAAGCCGAGTACTGGAACAGCCAGAAG
GACATCATGGAGCGGGTGCGGGCCGAGGTGGACACGGTGTGCAGACACAACCTACCAGGCA
GAGCTCATCACCTCCTTGCGAG

>ENA|HQ728667|HQ728667.1 Ovis aries clone DQB-B MHC class II antigen (DQB) mRNA, partial cds.
CTGGTCCAGTTTAAGGGCCTGTGTTACTTTCACCAACGGGACGGAGCGGGTGCGGAGTGTG
ACCAGATACATCTACAACCGGGAGGAGTACGTGCGCTTCGACAGCGACTGGGACGAGTAC
CGGGCGGTGACGCCGCTGGGGCGGCCGTCCGCCGAGTACTGGAACAGCCAGAAGGACATC
CTGGAGCAGACGCGGGCCGAGGTGGACACGGTGTGCAGACACAACCTACCAGGTGGATGCC

CCCTTCACCTGGCAGCGGCGAGTGGAACCTACAGTGACCGTCTCCCCGTCCAGGACTGAG
GCTCTAAACCACCACAACCTGCTGGTCTGCTCGGTGACGGATTCTATCCAGGCCAGATC
AAGGTTTCGGTGGTTCCGGAATGACCGGGAGGAGACAGCTGGAGTTGTGTCCACCCCTCTT
ATTAGGAATGGGACTGGACCTTCCAGATCCTCGTGATGCTGGAAATGACCCCCAGCGA
GGAGATGTGTACACCTGCCGCGTGGAGCACCCCAGCCTCCAGAGCCCCATCACGGTGGAG
TGGAGGGCACAGTCTGAATCTGCCCAGAGCAAGAT

>ENA|LN811403|LN811403.1 Ovis aries partial DQB1 gene for MHC class II
antigen, allele DQB1*8t040, exon 2
TTCCAGTTTAAGGGCCTGTGTTACTTCACCAACGGGACGGAGCGGGTGCGGCTCGTGACC
AGATACTTCTACAACCGGGAGGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGG
GCGGTGACGCCGCTGGGGCGGCCGTCCGCCGAGTACTGGAACAGCCAGAAGGACATCCTG
GAGCAGACGCGGGCCGAGGTGGACACGGTGTGCAGACACAACCTACCAGGTGGATGCCC

>ENA|LN811404|LN811404.1 Ovis aries partial DQB1 gene for MHC class II
antigen, allele DQB1*9t027, exon 2
GTCCAGTTAAAGGGCCTGTGTTACTTCACCAACGGGACGGAGCGGGTGCGGCTCGTGACC
AGATACATCTACAACCGGCAAGAGGACGTGCGCTTCGACAGCGACTGGGGCGAGTACCGC
GGGGTGACCCCGCTGGGGCGGCCGGAAGCCGAGTACTGGAACAGCCAGAAGGACATCCTG
GAGCAGACGCGGGCCGAGGTGGACACGGTGTGCAGAAACAACCTACCAGGTGGATGCCC

>ENA|LN810546|LN810546.1 Ovis aries partial DQB1 gene for MHC class II
antigen, allele DQB1*94.y164, exon 2
TACCAGTTTAAGGGCCTGTGTTACTTCACCAACGGGACGGAGCGGGTGCGGCTCGTGACC
AGATACTTATAACAACCGGGAGGAGTTCTGTCGCTTCGACAGCGACTGGGGCGAGTACCGG
GGGGTGACGCCGCCGGGGCAGCGGCAAGCCGAGTACTGGAACAGCCAGAAGGACATCCTG
GAGCGGACGCGGGCCGAGGCGGACACGGTGTGCAGACACAACCTACCGGGTGCATGCCC

>ENA|LN810547|LN810547.1 Ovis aries partial DQB1 gene for MHC class II
antigen, allele DQB1*94.b076, exon 2
TTTCTGTTTATGGGCCAGTGTTACTTCACCAACGGGACGGAGCGGGTGCGGCTCGTGACC
AGATACATCTACAACCAGGAAGAGCACCTGCGCTTCGACAGCGACTGGGGCGAGTACCGG
GCGGTGACGCCGCCGGGGCAGCGGCAAGCCGAGTACTTCAACAGCCAGAAGGACATCCTG
GAGCGGACGCGGGCCGAGGCGGACACGGTGTGCAGACACAACCTACCAGGTGGAAGCCG

>ENA|GU191453|GU191453.1 Ovis aries MHC class II antigen (Ovar-DQB) gene,
Ovar-DQB*New1 allele, exon 2 and partial cds.
CACCAGTTTAAGGGCCAGTGTTACTTCACCAACGGGACGGAGCGGGTGCGGCATGTGACC
AGATACATCTACAACCGGGAGGAGTACGCGCGCTTCGACAGCGACTGGGGACGAGTACCGG
GCGGTGACGCCGCTGGGGCGGCCGACGCCGAGTACTGGAACAGCCAGAAGGACTTCCTG
GAGCAGACGCGGGCCGAGGTGGACAGGGTGTGCAGACACAACCTACCGGGTGTATGCCCCC
TTCACCTGGCAGCGGCGAGGT

>ENA|GU191454|GU191454.1 Ovis aries MHC class II antigen (Ovar-DQB) gene,
Ovar-DQB*New6 allele, exon 2 and partial cds.
GTCCAGTTTAAGTGCCACTGTTACTTCACCAACGGGACGGAGCGGGTGCGGTACGTGACC
AGATACATCTACAACCGGCAGGAGGACGTGCGCTTCGACAGCGACTGGAACGAGTACCGG
GCGGTGACGCCGCTGGGGCGGCCGACGCCGAGTACTGGAACAGCCAGAAGGACATCCTG
GAGCAGACGCGGGCCGAGGCGGACACGGTGTGCAGACACAACCTACCGGGTGCATGCCCCC
TTCACCTGGCAGCGGCGAGGT

>ENA|GU191455|GU191455.1 Ovis aries MHC class II antigen (Ovar-DQB) gene,
Ovar-DQB*Tnew1 allele, exon 2 and partial cds.
TTTCTGTTTATGGGCCAGTGTTACTTCACCAACGGGACGGAGCGGGTGCGGCTCGTGACC
AGATACATCTACAACCAGGAAGAGCACCTGCGCTTCGACAGCGACTGGGGCGAGTACCGG
GCGGTGACGCCGCTGGGGCGGCCGACGCCGAGTACTTCAACAGCCAGAAGGACATCCTG
GAGCGGACGCGGGCCGAGGCGGACACGGTGTGCAGACACAACCTACCAGGTGGAAGCCGCC
TTCACCTGGCAGCGGCGAGGT

>ENA|GU191456|GU191456.1 Ovis aries MHC class II antigen (Ovar-DQB) gene,
Ovar-DQB*Tnew3 allele, exon 2 and partial cds.
TACCAGTTTAAGGGCCTGTGTTACTTCACCAACGGGACGGAGCGGGTGCGGCTCGTGACC
AGACACATCTACAACCGGGAGGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCGG

GCGGTGACGCCCGGGGAGCGGCAAGCCGAGTACTGGAACAGCCAGAAGGACATCATG
GAGCGGGTGCAGGGCCGAGGTGGACACGGTGTGCAGAAACAACCTACCGGGTGTATGCCCCC
TTCACCTGGCAGCGGCGAGGT

>ENA|GU191459|GU191459.1 Ovis aries MHC class II antigen (Ovar-DQB) gene,
Ovar-DQB*4389_4 allele, exon 2 and partial cds.

GTCCAGTTTTAAGTGCCACTGTTACTTCACCAACGGGACGGAGCGGGTGCGGTACGTGACC
AGATACATCTACAACCGGGAGGAGTACGCGCGCTTCGACAGCGACTGGGACGAGTACCGC
GGGGTGACGCCCGGGGAGCGGCAAGCCGAGTACTGGAACAGCCAGAAGGACATCCTG
GAGCGGACGCGGGCCGAGGTGGACACGGTGTGCAGAAACAACCTACCGGGTGTATGCCCCC
TTCACCTGGCAGCGGCGAGGT

>ENA|GU191460|GU191460.1 Ovis aries MHC class II antigen (Ovar-DQB) gene,
Ovar-DQB*13a allele, exon 2 and partial cds.

CACCAGTTTTAAGGGCCAGTGTTACTTCACCAACGGGACGGAGCGGGTGCGGCTCGTGACC
AGATACATCTACAACCGGGAGGAGTACGCGCGCTTCGACAGCGACTGGGACGAGTACCGG
GCGGTGACGCCCGCTGGGGCGGGCCGACGCCGAGTACTGGAACAGCCAGGAGGACATCATG
GAGCGGACGCGGGCCGAGGTGGACAGGGTGTGCAGACACAACCTACCGGGTGTATGCCCCC
TTCA

>ENA|Z28423|Z28423.1 O.aries (cluster 2B) MHC class II DQB1 gene, exon 2.

CCCGGGTTCGCAGCGGGAGGCGCAGGGCCCGCTGGAGCGGGACAGGGCCTGAGCGACGG
GTTTCAGGTTTAGGGACCCCGCTGGCGGGCTCGGCACGTCCCCATCTGGCCGAGCGGCC
CCGCGTGGGGCTGTGGGGCTGAGCCTGACCGAGCGGCTGTCTCCCCGCAGAGGATTTCTGT
GCACCAAGTTTATAGGCCAGTGTTACTTCACCAACGGGACGGAGCGGGTGCGGCTCGTGAC
CAGATACATCTACAACAGGAGGAGTTCTGTGCGCTTCGACAGCGACTGGGACGAGTACCG
GGCGGTGACCCCGCTGGGGCGGGCGGCACGCCGAGTACTTCAACAGCCAGAAGGACATCCT
GGAGCAGACGCAGGCCGCGGTGGACACGGTGTGCAGAAACAACCTACCAGGTGGAAGCCGC
CTTCACCTGGCAGCGGCGAGGTGAGTGCCGGCCGCCCTCCGCGGGCCCGCCCTCCACCCG
CCAGGACTCCGCACCGAAGGA

Goat

>ENA|AY464658|AY464658.1 Capra hircus major histocompatibility class II
DQB1 (Cahi-DQB1) gene, Cahi-DQB1.1 allele, exon 2 and partial cds.

AGGATTTTCGTGGTCCAGTTTAAGGGCCTGTGTTACTTCACCAACGGGACGGAGCGGGTGC
GGCTCGTGACAGATACATCTACAACAGGAGGAGTACGCGCGCTTCGACAGCGACTGGG
GCGAGTACCGGGCGGTGACGCCGCTGGGGCGGCCGAGTACTGGAACAGCCAGG
AGGACATCCTGGAGCAGACGCGGGCCGAGGTGGACAGGGTGTGCAGACACAACCTACCAGG
TGGAAGCCGCCTTCACCTGGCAGCGGCGAG

>ENA|AY464659|AY464659.1 Capra hircus major histocompatibility class II
DQB1 (Cahi-DQB1) gene, Cahi-DQB1.5 allele, exon 2 and partial cds.

AGGATTTTCGTGGTCCAGTTCAAGGGCCTGTGTTACTTCACCAACGGGACGGAGCGGGTGC
GGCTCGTGACAGATACATCTACAACCGGGAGGAGTACGCGCGCTTCGACAGCGACTGGG
GCGAGTACCGGGCGGTGACGCCGCTGGGGCGGCCGAGTACTGGAACAGCCAGG
AGGACATCCTGGAGCGGACGCGGGCCGAGGTGGACAGGGTGTGCAGACACAACCTACCGGG
TGTATGCCCCCTTCACCTGGCAGCGGCGAG

Cattle

>ENA|U77795|U77795.1 Bos taurus major histocompatibility complex class II
DQB2 gene (DQB2*1 allele), exon 2 and partial cds.

GGTCCAGTTTATGGGCCAGTGTTATTTACCAACGGGACGGAGCGGGTGCGGTACGTGAC
CAGATACATCTACAACAGGAGGAGTACGCGCGCTTCGACAGCGACTGGGGCGAGTACCG
GGCGCTGACCCCGCTGGGGCGGCCGCGCCGAGTACTGGAACAGCCAGAAGGACATCCT
GGAGCAGACGTGGGCCGAGGTGGACAGGGTGTGCAGAAACAACCTACCAGGTGGAAGCCCC
CTTC

>ENA|U77796|U77796.1 Bos taurus major histocompatibility complex class II DQB2 gene (DQB2*2A allele), exon 2 and partial cds.
GTACCAGTTTATGGGCCAGTGTTATTTACCAACGGGACGGAGCGGGTGCGGTACGTGAC
CAGATACATCTACAACCAGGAGGAGTACGCGCGCTTCGACAGCGACTGGGACGAGTACCG
GGCGCTGACCCCGCTGGGGCGGCCGGCCGCCGAGTACTGGAACAGCCAGAAGGACATCCT
GGAGCGGACGCGGGCCGAGGTGGACAGGGTGTGCAGAAACAACCTACCAGGTGGAAGCCCC
CTTC

>ENA|U77797|U77797.1 Bos taurus major histocompatibility complex class II DQB2 gene (DQB2*2B allele), exon 2 and partial cds.
GTACCAGTTTATGGGCCAGTGTTATTTACCAACGGGACGGAGCGGGTGCGGTACGTGAC
CAGATACATCTACAACCAGGAGGAGTACGCGCGCTTCGACAGCGACTGGGACGAGTACCG
GGCGCTGACCCCGCTGGGGCGGCCGGCCGCCGAGTACTGGAACAGCCAGAAGGACATCCT
GGAGCGGACGCGGGCCGAGGTGGACAGGGTGTGCAGAAACAACCTACCAGGTGGATGCCCC
CTTC

>ENA|U77798|U77798.1 Bos taurus major histocompatibility complex class II DQB2 gene, (DQB2*3 allele), exon 2 and partial cds.
GTTCCAGTTTATGGGCCAGTGTTATTTACCAACGGGACGGAGCGGGTGCGGTACGTGAC
CAGATACATCTACAACCAGGAGGAGTTTCGCGCGCTTCGACAGCGACTGGGACGAGTACCG
GGCGGTGACCCCGCTGGGGCGGCCGGACGCCGAGCTCTGGAACAGCCAGAAGGACATCCT
GGAGCGGACGCGGGCCGAGGTGGACAGGGTGTGCAGAAACAACCTACCAGGTGGATGCCCC
CTTC

Appendix 5: List of Submitted Sequences to EBI

Gene	Local Name	Gene Accession Name
DQA1	92.y085	LN736359
	HE574809	LN827890
	extendedZ28518	LN827891
	8t036	LN827892
	96.y200	LN827893
	extendedZ28418	LN827894
	extendedHQ728659	LN827895
DQB1	94.y164	LN810546
	94.b076	LN810547
	8t040	LN811403
	9t027	LN811404
DQB2	8t013	LN868258
	8t023	LN868259
	0t041	LN868260
	0t175	LN868261
	8t006	LN868264

LN736359; SV 1; linear; genomic DNA; STD; MAM; 442 BP.

XX

AC LN736359;

XX

DT 06-FEB-2015 (Rel. 123, Created)

DT 06-FEB-2015 (Rel. 123, Last updated, Version 1)

XX

DE Ovis aries partial Ovar-DQA1 gene for MHC class II antigen, allele

DE Ovar-DQA1*92.y085, exon 2

XX

KW .

XX

OS Ovis aries (sheep)

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia;

OC Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;

OC Caprinae; Ovis.

XX

RN [1]

RP 1-442

RA Md Isa N.;

RT ;

RL Submitted (18-DEC-2014) to the INSDC.

RL College of Medical, Veterinary and Life Sciences, , University of Glasgow,

RL Gene and Protein Laboratory, G611QH, UNITED KINGDOM.

XX

RT "Variation in the sheep MHC-DQA1 locus";

```

RL   Unpublished.
XX
DR   MD5; ele4fe72dbe5f7876aae6309aa70a24a.
XX
FH   Key                      Location/Qualifiers
FH
FT   source                    1..442
FT                               /organism="Ovis aries"
FT                               /mol_type="genomic DNA"
FT                               /PCR_primers="fwd_name: NikDQA1F, fwd_seq:
FT                               actggccacaaatgaagcccactggccacaaatgaagcccacaaacaa,
rev_name:
FT                               NikDQA1R, rev_seq: agaaggcagaagatgaggggttcag"
FT                               /db_xref="taxon:9940"
FT   intron                    <1..49
FT                               /gene="Ovar-DQA1"
FT                               /allele="Ovar-DQA1*92.y085"
FT                               /number=1
FT   CDS                       <50..>298
FT                               /codon_start=3
FT                               /gene="Ovar-DQA1"
FT                               /allele="Ovar-DQA1*92.y085"
FT                               /product="MHC class II antigen"
FT                               /function="antigen presenting molecule"
FT                               /db_xref="GOA:A0A0B7D202"
FT                               /db_xref="InterPro:IPR001003"
FT                               /db_xref="InterPro:IPR011162"
FT                               /db_xref="InterPro:IPR014745"
FT                               /db_xref="UniProtKB/TrEMBL:A0A0B7D202"
FT                               /protein_id="CEL26672.1"
FT
FT   /translation="DHIAAYGINVYHSYGPSGYTTFEFDGDEEFYVDLEKRETVWRLPV
FT                               FSQFRRFDPQGALRNIAVGKQSLEILIQRSNSTAATN"
FT   exon                      50..298
FT                               /gene="Ovar-DQA1"
FT                               /allele="Ovar-DQA1*92.y085"
FT                               /number=2
FT   intron                    299..>442
FT                               /gene="Ovar-DQA1"
FT                               /allele="Ovar-DQA1*92.y085"
FT                               /number=2
XX
SQ   Sequence 442 BP; 103 A; 115 C; 84 G; 140 T; 0 other;
    gaggatattt tctctatttt tccctttctt gctcctcact ccgactcagc tgaccacatt
60   gccgcctatg gcataaatgt ctaccactca tatgggtccct ctggctacta tacccatgaa
120  tttgatggag atgaagagtt ctacgtggac ctggaaaaga gggagactgt ctggcgtctg
180  cctgtgttta gtcaatttag aaggtttgat cctcaggggtg cactgagaaa catcgctgtg
240  gggaaacagt ctttggagat cttgattcaa aggtccaact ctactgctgc taccaacagt
300  aagtgttcgc cattctgcct ctctttatta atctaccctt tcatgccagc ttcactccct
360  ttttctctag ggatagatac ccttcaccgc tttataaaaa ctctctcctt tccaaggaca
420  ccacattttc tcatggtaat ag
442
//

```

ID LN827890; SV 1; linear; genomic DNA; STD; MAM; 477 BP.
 XX
 AC LN827890;
 XX
 DT 14-MAR-2015 (Rel. 124, Created)
 DT 14-MAR-2015 (Rel. 124, Last updated, Version 1)
 XX
 DE Ovis aries partial Ovar-DQA1 gene for MHC class II antigen, allele
 DE Ovar-DQA1*extendedHE574809, exon 2
 XX
 KW .
 XX
 OS Ovis aries (sheep)
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia;
 OC Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora;
 Bovidae;
 OC Caprinae; Ovis.
 XX
 RN [1]
 RP 1-477
 RA Md Isa N.;
 RT ;
 RL Submitted (24-FEB-2015) to the INSDC.
 RL College of Medical, Veterinary and Life Sciences, University of
 Glasgow,
 RL Gene and Protein Laboratory, G611QH, UNITED KINGDOM.
 XX
 RT "Variation in the sheep MHC-DQA1 locus";
 RL Unpublished.
 XX
 DR MD5; fe2b230404a01ffd5af4abc735bfbbb9.
 XX

FH	Key	Location/Qualifiers
FH		
FT	source	1..477
FT		/organism="Ovis aries"
FT		/mol_type="genomic DNA"
FT		/PCR_primers="fwd_name: NikDQA1F, fwd_seq:
FT		actggccacaaatgaagcccacaa, rev_name: NikDQA1R,
	rev_seq:	
FT		agaaggcagaagatgaggggttcag"
FT		/db_xref="taxon:9940"
FT	CDS	<88..>333
FT		/codon_start=1
FT		/transl_table=1
FT		/gene="Ovar-DQA1"
FT		/allele="Ovar-DQA1*extendedHE574809"
FT		/product="MHC class II antigen"
FT		/function="antigen presenting molecule"
FT		/db_xref="GOA:A0A0D6ETY5"
FT		/db_xref="InterPro:IPR001003"
FT		/db_xref="InterPro:IPR011162"
FT		/db_xref="InterPro:IPR014745"
FT		/db_xref="UniProtKB/TrEMBL:A0A0D6ETY5"
FT		/protein_id="CEV42181.1"
FT		
	/translation="DHIAAYGINVYHKYGPSGYTTFDGDDEEFYVDLEKRETVVHLP	
FT		FSKFRRFDPQGALRNIAAAKHNLEVLIQDSNSTAASN"
FT	exon	88..333
FT		/gene="Ovar-DQA1"
FT		/allele="Ovar-DQA1*extendedHE574809"
FT		/number=2

```

XX
SQ      Sequence 477 BP; 116 A; 121 C; 81 G; 159 T; 0 other;
        tgtttgatag tcaatttctt ctttcacttg cttaatgagg atcttctctc tatttttccc
60
        tttcttgctc ctcaccctga ctcagctgac cacattgctg cctatggcat aaacgtctac
120
        cacaaatatg gtccctctgg ctactatacc catgaatttg atggagatga agagttctac
180
        gtggacctgg aaaagcgggg gactgtctgg catctgcccc tgtttagtaa atttagacgt
240
        tttgaccctc aggggtgcact gagaaacata gctgcagcga aacataatth ggaggtcttg
300
        attcaagatt ccaactctac tgctgctagc aacagtaagt gttcaccatt ttgcctctct
360
        ttattaatct accccttcat accagcttca ctcccttttt ctctagggat agataccctt
420
        cactgcttta taaaactctc tcctttccaa ggataccaca ttttctcatg gtaatag
477
//

ID      LN827891; SV 1; linear; genomic DNA; STD; MAM; 467 BP.
XX
AC      LN827891;
XX
DT      14-MAR-2015 (Rel. 124, Created)
DT      14-MAR-2015 (Rel. 124, Last updated, Version 1)
XX
DE      Ovis aries partial Ovar-DQA1 gene for MHC class II antigen, allele
DE      Ovar-DQA1*extendedZ28518, exon 2
XX
KW      .
XX
OS      Ovis aries (sheep)
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia;
OC      Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora;
Bovidae;
OC      Caprinae; Ovis.
XX
RN      [1]
RP      1-467
RA      Md Isa N.;
RT      ;
RL      Submitted (27-FEB-2015) to the INSDC.
RL      College of Medical, Veterinary and Life Sciences, , University of
Glasgow,
RL      Gene and Protein Laboratory, G611QH, UNITED KINGDOM.
XX

RT      "Variation in the sheep MHC-DQA1 locus";
RL      Unpublished.
XX
DR      MD5; 9ff1248e2ca00784554a4dd04b73b4ee.
XX
FH      Key          Location/Qualifiers
FH
FT      source          1..467
FT                      /organism="Ovis aries"
FT                      /mol_type="genomic DNA"
FT                      /PCR_primers="fwd_name: NikDQA1F, fwd_seq:
FT                      actggccacaaatgaagcccacaa, rev_name: NikDQA1R,
rev_seq:
FT                      agaaggcagaagatgagggttcag"

```

```

FT          /db_xref="taxon:9940"
FT   CDS      <79..>325
FT          /codon_start=1
FT          /transl_table=1
FT          /gene="Ovar-DQA1"
FT          /allele="Ovar-DQA1*extendedZ28518"
FT          /product="MHC class II antigen"
FT          /function="antigen presenting molecule"
FT          /db_xref="GOA:A0A0D6ET06"
FT          /db_xref="InterPro:IPR001003"
FT          /db_xref="InterPro:IPR011162"
FT          /db_xref="InterPro:IPR014745"
FT          /db_xref="UniProtKB/TrEMBL:A0A0D6ET06"
FT          /protein_id="CEV42182.1"
FT
FT /translation="DHIAAYGINVYHSYGPSGYTTFDGDDEEFYVDLEKRETVWHLPV
FT          FSQFRSFDPPQALRNIAIVKHNLEVLIQRSNSTAATN"
FT   exon      79..325
FT          /gene="Ovar-DQA1"
FT          /allele="Ovar-DQA1*extendedZ28518"
FT          /number=2
XX
SQ   Sequence 467 BP; 112 A; 122 C; 80 G; 153 T; 0 other;
    gtcaatttct tctttcactt gcttaatgag gatcttttct ctatttttcc ctttcttgct
60
    cctcactcca actcagctga ccacattgcc gcctatggca taaatgtcta ccactcatat
120
    ggtccctctg gctactatac ccatgaattt gatggagatg aagagttcta cgtggacctg
180
    gaaaagaggg agactgtctg gcatctgcct gtgttttagtc aatttagaag ttttgaccct
240
    caggggtgcac tgagaaacat agctacggtg aaacataatt tggaggtcct gattcaaagg
300
    tccaactcta ctgctgctac caacagtaag tggtcaccat tctgcctctc tttattaatc
360
    tacccttca tgccagcttc actccctttt tctctaggga tagataccct tcaccgcttt
420
    ataaaactct ctcttccaa ggacaccaca ttttctcatg gtaatag
467
//
ID   LN827892; SV 1; linear; genomic DNA; STD; MAM; 476 BP.
XX
AC   LN827892;
XX
DT   14-MAR-2015 (Rel. 124, Created)
DT   14-MAR-2015 (Rel. 124, Last updated, Version 1)
XX
DE   Ovis aries partial Ovar-DQA1 gene for MHC class II antigen, allele
DE   Ovar-DQA1*8t036, exon 2
XX
KW   .
XX
OS   Ovis aries (sheep)
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia;
OC   Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora;
Bovidae;
OC   Caprinae; Ovis.
XX
RN   [1]
RP   1-476
RA   Md Isa N.;
RT   ;

```

```

RL   Submitted (27-FEB-2015) to the INSDC.
RL   College of Medical, Veterinary and Life Sciences, , University of
Glasgow,
RL   Gene and Protein Laboratory, G611QH, UNITED KINGDOM.
RT   "Variation in the sheep MHC-DQA1 locus";
RL   Unpublished.
XX
DR   MD5; 91412c082fa94df000d9dd189a7b1479.
XX
FH   Key                      Location/Qualifiers
FH
FT   source                    1..476
FT                               /organism="Ovis aries"
FT                               /mol_type="genomic DNA"
FT                               /PCR_primers="fwd_name: NikDQA1F, fwd_seq:
FT                               actggccacaaatgaagcccacaa, rev_name: NikDQA1R,
rev_seq:
FT                               agaaggcagaagatgagggttcag"
FT                               /db_xref="taxon:9940"
FT   CDS                       <85..>330
FT                               /codon_start=1
FT                               /transl_table=1
FT                               /gene="Ovar-DQA1"
FT                               /allele="Ovar-DQA1*8t036"
FT                               /product="MHC class II antigen"
FT                               /function="antigen presenting molecule"
FT                               /db_xref="GOA:A0A0D6ETS7"
FT                               /db_xref="InterPro:IPR001003"
FT                               /db_xref="InterPro:IPR011162"
FT                               /db_xref="InterPro:IPR014745"
FT                               /db_xref="UniProtKB/TrEMBL:A0A0D6ETS7"
FT                               /protein_id="CEV42183.1"
FT
FT   /translation="DHIAAYGINVYHSYGPSGYTTFEFDGDEQFYVDLEKKETVWRLPE
FT   FSKFTSFDPQGALRNMASGKQTLEIMIQRSNSTAATN"
FT   exon                      85..330
FT                               /gene="Ovar-DQA1"
FT                               /allele="Ovar-DQA1*8t036"
FT                               /number=2
XX
SQ   Sequence 476 BP; 114 A; 125 C; 83 G; 154 T; 0 other;
    tgttgatagt caattcttct ttcactgctt aatgaggatc ttttctctat ttttcccttt
60
    cttgctcttc actccgactc agctgaccac attgccgcct atggcataaa cgtctaccac
120
    tcatatggtc cctctggcta ctatacccat gaatttgatg gagatgaaca gttctacgtc
180
    gacctggaaa agaaggagac tgtctggcgt ctgcctgagt ttagtaaatt tacaagtttt
240
    gaccctcagg gtgcactgag aaacatggcg tcggggaaac agactttgga gatcatgatt
300
    caaaggtcca actctactgc tgctaccaac agtaagtgtt caccattctg cctctcttta
360
    ttaatcttcc ccttcatgcc agcttcactc cctttttccc tagggataga tacccttcac
420
    cactttataa aactttctcc tttccaagga gtcaccatat tttctcatgg taatag
476
//

ID   LN827893; SV 1; linear; genomic DNA; STD; MAM; 465 BP.
XX
AC   LN827893;
XX

```


DT 20-MAR-2015 (Rel. 124, Created)
 DT 20-MAR-2015 (Rel. 124, Last updated, Version 1)
 XX
 DE Ovis aries partial Ovar-DQA1 gene for MHC class II antigen, allele
 DE Ovar-DQA1*96.y200, exon 2
 XX
 KW .
 XX
 OS Ovis aries (sheep)
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia;
 OC Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora;
 Bovidae;
 OC Caprinae; Ovis.
 XX
 RN [1]
 RP 1-465
 RA Md Isa N.;
 RT ;
 RL Submitted (28-FEB-2015) to the INSDC.
 RL College of Medical, Veterinary and Life Sciences, , University of
 Glasgow,
 RL Gene and Protein Laboratory, G611QH, UNITED KINGDOM.
 XX
 RT "Variation in the sheep MHC-DQA1 locus";
 RL Unpublished.
 XX
 DR MD5; 9ea2dac1859d91badc6ccdfc7690f3a9.
 XX
 FH Key Location/Qualifiers
 FH
 FT source 1..465
 FT /organism="Ovis aries"
 FT /mol_type="genomic DNA"
 FT /PCR_primers="fwd_name: NikDQA1F, fwd_seq:
 FT actggccacaaatgaagcccacaa, rev_name: NikDQA1R,
 rev_seq:
 FT agaaggcagaagatgaggggttcag"
 FT /db_xref="taxon:9940"
 FT CDS <76..>321
 FT /codon_start=1
 FT /transl_table=1
 FT /gene="Ovar-DQA1"
 FT /allele="Ovar-DQA1*96.y200"
 FT /product="MHC class II antigen"
 FT /function="antigen presenting molecule"
 FT /db_xref="GOA:A0A0D6ETG3"
 FT /db_xref="InterPro:IPR001003"
 FT /db_xref="InterPro:IPR011162"
 FT /db_xref="InterPro:IPR014745"
 FT /db_xref="UniProtKB/TrEMBL:A0A0D6ETG3"
 FT /protein_id="CEV42184.1"
 FT
 /translation="DHIGTYGVNVYQTYGSSGYTTFEFDGDEQFYVDLEKRETVWRLPM
 FT FSEVGYFDAQFALRNIAATFKHNLELMIQRSNSTAATN"
 FT exon 76..321
 FT /gene="Ovar-DQA1"
 FT /allele="Ovar-DQA1*96.y200"
 FT /number=2
 XX
 SQ Sequence 465 BP; 114 A; 121 C; 76 G; 154 T; 0 other;
 aattttcttct ttactgtctt taatgaagat cttttctcta tttttccctt tcttgctcct
 60

```

120 caccctgact cagctgacca cattggcacc tatggcgtaa acgtctacca aacatatggt
180 tcttctggct actataccca tgaatttgat ggagatgaac aattctacgt ggacctggaa
240 aagcgggaga ctgtctggcg tctacctatg tttagtgaag ttggatattt tgacgctcag
300 tttgcactga gaaacatagc tacgttcaaa cataatttgg agctcatgat tcagaggtcc
360 aactctactg ctgctaccaa cagtatgtgt tcaccattct gcctctcttt attaacttac
420 ccttcaaacc aggcctcact cccttttccc ctagggataa gtacccttca ccactttata
465 aaactctctc ctttccaagg acaccatggt ttctcttggt aatag
//

```

```

ID LN827894; SV 1; linear; genomic DNA; STD; MAM; 471 BP.
XX
AC LN827894;
XX
DT 14-MAR-2015 (Rel. 124, Created)
DT 14-MAR-2015 (Rel. 124, Last updated, Version 1)
XX
DE Ovis aries partial Ovar-DQA1 gene for MHC class II antigen, allele
DE Ovar-DQA1*extendedZ28418, exon 2
XX
KW .
XX
OS Ovis aries (sheep)
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia;
OC Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora;
Bovidae;
OC Caprinae; Ovis.
XX
RN [1]
RP 1-471
RA Md Isa N.;
RL Submitted (01-MAR-2015) to the INSDC.
RL College of Medical, Veterinary and Life Sciences, , University of
Glasgow,
RL Gene and Protein Laboratory, G611QH, UNITED KINGDOM.
XX
RL Unpublished.
XX
DR MD5; fe2ebaee63d914fcb9e22ebaa31b238e.
XX
FH Key Location/Qualifiers
FH
FT source 1..471
FT /organism="Ovis aries"
FT /mol_type="genomic DNA"
FT /PCR_primers="fwd_name: NikDQA1F, fwd_seq:
FT actggccacaaatgaagcccacaa, rev_name: NikDQA1R,
rev_seq:
FT agaaggcagaagatgagggttcag"
FT /db_xref="taxon:9940"
FT CDS <79..>324
FT /codon_start=1
FT /transl_table=1
FT /gene="Ovar-DQA1"
FT /allele="Ovar-DQA1*extendedZ28418"
FT /product="MHC class II antigen"

```

```

FT          /function="antigen presenting molecule"
FT          /db_xref="GOA:A0A0D6EUF7"
FT          /db_xref="InterPro:IPR001003"
FT          /db_xref="InterPro:IPR011162"
FT          /db_xref="InterPro:IPR014745"
FT          /db_xref="UniProtKB/TrEMBL:A0A0D6EUF7"
FT          /protein_id="CEV42185.1"
FT
XX
SQ          /translation="DHIGIYGVNQYQTYGPSGYTTFDGDDEEFYVDLEKRETVWRLPE
FT          FSKFTSFDPQGALRNIAAKHNLEILIQMSNSTAATN"
FT          exon          79..324
FT          /gene="Ovar-DQA1"
FT          /allele="Ovar-DQA1*extendedZ28418"
FT          /number=2
XX
SQ          Sequence 471 BP; 113 A; 124 C; 80 G; 154 T; 0 other;
          gtccaatttc ttctttcact gcttaatgag gatcttttct ctatttttcc ctttcttgct
60
          cctcaccctg actcagctga ccacattggc atctatggcg taaacgtcta ccaaacatat
120
          ggtccctctg gctactatac ccatgaatth gatggagatg aagagttcta cgtggacctg
180
          gaaaagaggg agactgtctg gcgtctgcct gagtttagta aatttacaag ttttgaccct
240
          caggggtgcac tgagaaacat agctacggcg aaacataatt tggagatctt gattcaaagt
300
          tccaactcta ctgctgtac caacagtagc tggtcaccat tctgcctctc tttgttgctc
360
          ttcccccttca taccagcttc actccctttt tccctagggg tagataccct tcaccactct
420
          ataaaacttt ctcctttcca aggagtcacc acattttctc atggtaaata t
471
//

ID          LN827895; SV 1; linear; genomic DNA; STD; MAM; 475 BP.
XX
AC          LN827895;
XX
DT          20-MAR-2015 (Rel. 124, Created)
DT          20-MAR-2015 (Rel. 124, Last updated, Version 1)
XX
DE          Ovis aries partial Ovar-DQA1 gene for MHC class II antigen, allele
DE          Ovar-DQA1*extendedHQ728659, exon 2
XX
KW          .
XX
OS          Ovis aries (sheep)
OC          Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia;
OC          Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora;
Bovidae;
OC          Caprinae; Ovis.
XX
RN          [1]
RP          1-475
RA          Md Isa N.;
RT          ;
RL          Submitted (28-FEB-2015) to the INSDC.
RL          College of Medical, Veterinary and Life Sciences, , University of
Glasgow,
RL          Gene and Protein Laboratory, G611QH, UNITED KINGDOM.
XX
RT          "Variation in the sheep MHC-DQA1 locus";

```

```

RL   Unpublished.
XX
DR   MD5; 33be1c86e51f46a6ac1de3e17c167e8f.
XX
FH   Key                      Location/Qualifiers
FH
FT   source                    1..475
FT                               /organism="Ovis aries"
FT                               /mol_type="genomic DNA"
FT                               /PCR_primers="fwd_name: NikDQA1F, fwd_seq:
FT                               actggccacaaatgaagcccacaa, rev_name: NikDQA1R,
rev_seq:
FT                               agaaggcagaagatgaggggttcag"
FT                               /db_xref="taxon:9940"
FT   CDS                       <85..>330
FT                               /codon_start=1
FT                               /transl_table=1
FT                               /gene="Ovar-DQA1"
FT                               /allele="Ovar-DQA1*extendedHQ728659"
FT                               /product="MHC class II antigen"
FT                               /function="antigen presenting molecule"
FT                               /db_xref="GOA:A0A0D6ETZ1"
FT                               /db_xref="InterPro:IPR001003"
FT                               /db_xref="InterPro:IPR011162"
FT                               /db_xref="InterPro:IPR014745"
FT                               /db_xref="UniProtKB/TrEMBL:A0A0D6ETZ1"
FT                               /protein_id="CEV42186.1"
FT
FT   /translation="DHIGTYGVNVYQTYGPSGYTTFEFDGDEEFYVDLEKRETVWRLPM
FT                               FSEVGYFDPQFALRNIAITFKHNLELMIQRSNSTAATN"
FT   exon                      85..330
FT                               /gene="Ovar-DQA1"
FT                               /allele="Ovar-DQA1*extendedHQ728659"
FT                               /number=2
XX
SQ   Sequence 475 BP; 114 A; 122 C; 82 G; 157 T; 0 other;
    ggatgggtcaa tttcttcttt cactttgctt aatgaggatc ttttctctat ttttcccttt
60
    cttgttcctc actctgactc agctgaccac attggcacct atggcgtaaa cgtctaccaa
120
    acatatggtc cctctggcta ctatacccat gaatttgatg gagatgaaga gttctacgtg
180
    gacctggaaa agagggagac tgtctggcgt ctacctatgt ttagtgaagt tggatatattt
240
    gaccctcagt ttgcactgag aaacatagct acgttcaaac ataatttgga gctcatgatt
300
    cagaggtcca actctactgc tgctaccaac agtatgtggt caccattctg cctctcttta
360
    ttaatctacc ccttcaaacc aggcctcact cccttttccc ctagggataa gtacccttca
420
    ccactttata aaactctctc ctttccaagg acaccatggt ttctcttggt aatag
475
//
ID   LN810546; SV 1; linear; genomic DNA; STD; MAM; 238 BP.
XX
AC   LN810546;
XX
DT   06-FEB-2015 (Rel. 123, Created)
DT   06-FEB-2015 (Rel. 123, Last updated, Version 1)
XX
DE   Ovis aries partial DQB1 gene for MHC class II antigen, allele
DQB1*94.y164,
DE   exon 2

```

```

XX
KW  .
XX
OS  Ovis aries (sheep)
OC  Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia;
OC  Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora;
Bovidae;
OC  Caprinae; Ovis.
XX
RN  [1]
RP  1-238
RA  Md Isa N.;
RT  ;
RL  Submitted (21-JAN-2015) to the INSDC.
RL  College of Medical, Veterinary and Life Science, University of
Glasgow,
RL  Gene and Protein Laboratory, G611QH, UNITED KINGDOM.
XX
RT  "Variation in the sheep MHC-DQB1 locus";
RL  Unpublished.
XX
DR  MD5; da9ce338e18b3b2c51d63d19ed0bc6e1.
XX
FH  Key          Location/Qualifiers
FH
FT  source          1..238
FT                  /organism="Ovis aries"
FT                  /mol_type="genomic DNA"
FT                  /PCR_primers="fwd_name: JM05, fwd_seq:
FT                  tccccgcagaggatttcgtg, rev_name: JM06, rev_seq:
FT                  ctccgccgtgccaggtgaagg"
FT                  /db_xref="taxon:9940"
FT  CDS             <1..>238
FT                  /codon_start=1
FT                  /transl_table=1
FT                  /gene="DQB1"
FT                  /allele="DQB1*94.y164"
FT                  /product="MHC class II antigen"
FT                  /function="antigen presenting molecule"
FT                  /db_xref="GOA:A0A0B7MS96"
FT                  /db_xref="InterPro:IPR000353"
FT                  /db_xref="InterPro:IPR011162"
FT                  /db_xref="InterPro:IPR014745"
FT                  /db_xref="UniProtKB/TrEMBL:A0A0B7MS96"
FT                  /protein_id="CEO90965.1"
FT
FT  /translation="YQFKGLCYFTNGTERVRLVTRYLYNREEFVRFDSDWGEYRGVTPP
FT                  GQRQAEYWNSQKDILERTRAEADTVCRHNYRVHA"
FT  exon            1..238
FT                  /gene="DQB1"
FT                  /allele="DQB1*94.y164"
FT                  /number=2
XX
SQ  Sequence 238 BP; 51 A; 65 C; 88 G; 34 T; 0 other;
    taccagttta agggcctgtg ttacttcacc aacgggacgg agcgggtgcg gctcgtgacc
60
    agatacttat acaaccggga ggagttcgtg cgcttcgaca gcgactgggg cgagtaccgg
120
    ggggtgacgc cgccggggca gcggaagcc gagtactgga acagccagaa ggacatcctg
180
    gagcggacgc gggccgagggc ggacacggtg tgcagacaca actaccgggt gcatgccc
238

```

```

//
ID   LN810547; SV 1; linear; genomic DNA; STD; MAM; 238 BP.
XX
AC   LN810547;
XX
DT   06-FEB-2015 (Rel. 123, Created)
DT   06-FEB-2015 (Rel. 123, Last updated, Version 1)
XX
DE   Ovis aries partial DQB1 gene for MHC class II antigen, allele
DQB1*94.b076,
DE   exon 2
XX
KW   .
XX
OS   Ovis aries (sheep)
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia;
OC   Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora;
Bovidae;
OC   Caprinae; Ovis.
XX
RN   [1]
RP   1-238
RA   Md Isa N.;
RT   ;
RL   Submitted (21-JAN-2015) to the INSDC.
RL   College of Medical, Veterinary and Life Sciences, University of
Glasgow,
RL   Gene and Protein Laboratory, G611QH, UNITED KINGDOM.
XX
RT   "Variation in the sheep MHC-DQB1 locus";
RL   Unpublished.
XX
DR   MD5; 180f50e10717645860f8fd9ead387460.
XX
FH   Key                Location/Qualifiers
FH
FT   source              1..238
FT                       /organism="Ovis aries"
FT                       /mol_type="genomic DNA"
FT                       /PCR_primers="fwd_name: JM05, fwd_seq:
FT                       tccccgcagaggatttcgtg, rev_name: JM06, rev_seq:
FT                       ctgcgcgctgccaggtgaagg"
FT                       /db_xref="taxon:9940"
FT   CDS                 <1..>238
FT                       /transl_table=1
FT                       /gene="DQB1"
FT                       /allele="DQB1*94.b076"
FT                       /product="MHC class II antigen"
FT                       /function="antigen presenting molecule"
FT                       /db_xref="GOA:A0A0B7MT53"
FT                       /db_xref="InterPro:IPR000353"
FT                       /db_xref="InterPro:IPR011162"
FT                       /db_xref="InterPro:IPR014745"
FT                       /db_xref="UniProtKB/TrEMBL:A0A0B7MT53"
FT                       /protein_id="CE090966.1"
FT
FT   /translation="FLFMGQCYFTNGTERVRLVTRYIYNQEEHLRFDSDWGEYRAVTPP
FT   GQRQAEYFNSQKDILERTRAEADTVCRHNYQVEA"
FT   exon                1..238
FT                       /gene="DQB1"
FT                       /allele="DQB1*94.b076"
FT                       /number=2

```

XX
SQ Sequence 238 BP; 54 A; 67 C; 83 G; 34 T; 0 other;
tttctgttta tgggccagtg ttacttcacc aacgggacgg agcgggtgcg gctcgtgacc
60 agatacatct acaaccagga agagcacctg cgcttcgaca gcgactgggg cgagtaccgg
120 gcggtgacgc cgccgggggca gcggcaagcc gagtacttca acagccagaa ggacatcctg
180 gagcggacgc gggccgagggc ggacacggtg tgcagacaca actaccaggt ggaagccg
238
//

ID LN811403; SV 1; linear; genomic DNA; STD; MAM; 238 BP.

XX

AC LN811403;

XX

DT 22-MAR-2015 (Rel. 124, Created)

DT 22-MAR-2015 (Rel. 124, Last updated, Version 1)

XX

DE Ovis aries partial DQB1 gene for MHC class II antigen, allele
DQB1*8t040,

DE exon 2

XX

KW .

XX

OS Ovis aries (sheep)

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia;

OC Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora;
Bovidae;

OC Caprinae; Ovis.

XX

RN [1]

RP 1-238

RA Md Isa N.;

RT ;

RL Submitted (03-FEB-2015) to the INSDC.

RL College of Medical, Veterinary and Life Sciences, , University of
Glasgow,

RL Gene and Protein Laboratory, G611QH, UNITED KINGDOM.

RT "Variation in the sheep MHC-DQB1 locus";

RL Unpublished.

XX

DR MD5; af505570232c8ebf11b6863e27a2883c.

XX

FH	Key	Location/Qualifiers
----	-----	---------------------

FH

FT	source	1..238
----	--------	--------

FT		/organism="Ovis aries"
----	--	------------------------

FT		/mol_type="genomic DNA"
----	--	-------------------------

FT		/PCR_primers="fwd_name: JM05, fwd_seq:
----	--	--

FT		tccccgcagaggatttcgtg, rev_name: JM06, rev_seq:
----	--	--

FT		ctcgccgctgccaggtgaagg"
----	--	------------------------

FT		/db_xref="taxon:9940"
----	--	-----------------------

FT	CDS	<1..>238
----	-----	----------

FT		/codon_start=1
----	--	----------------

FT		/transl_table=1
----	--	-----------------

FT		/gene="DQB1"
----	--	--------------

FT		/allele="DQB1*8t040"
----	--	----------------------

FT		/product="MHC class II antigen"
----	--	---------------------------------

FT		/function="antigen presenting molecule"
----	--	---

FT		/db_xref="GOA:A0A0D6E1P5"
----	--	---------------------------

FT		/db_xref="InterPro:IPR000353"
----	--	-------------------------------

```

FT          /db_xref="InterPro:IPR011162"
FT          /db_xref="InterPro:IPR014745"
FT          /db_xref="UniProtKB/TrEMBL:A0A0D6E1P5"
FT          /protein_id="CEP13136.1"
FT
FT /translation="FQFKGLCYFTNGTERVRLVTRYFYNNREEYARFDSWDWGEYRAVTPL
FT          GRPSAEYWNSQKDILEQTRAEDVTVCRHNYQVDA"
FT      exon          1..238
FT          /gene="DQB1"
FT          /allele="DQB1*8t040"
FT          /number=2
XX
SQ      Sequence 238 BP; 49 A; 67 C; 86 G; 36 T; 0 other;
      ttccagttaa agggcctgtg ttacttcacc aacgggacgg agcgggtgcg gctcgtgacc
60
      agatacttct acaaccggga ggagtacgcg cgcttcgaca gcgactgggg cgagtaccgg
120
      gcggtgacgc cgctggggcg gccgtccgcc gagtactgga acagccagaa ggacatcctg
180
      gagcagacgc gggccgaggt ggacacggtg tgcagacaca actaccaggt ggatgccc
238
//
ID      LN811404; SV 1; linear; genomic DNA; STD; MAM; 238 BP.
XX
AC      LN811404;
XX
DT      22-MAR-2015 (Rel. 124, Created)
DT      22-MAR-2015 (Rel. 124, Last updated, Version 1)
XX
DE      Ovis aries partial DQB1 gene for MHC class II antigen, allele
DQB1*9t027,
DE      exon 2
XX
KW      .
XX
OS      Ovis aries (sheep)
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia;
OC      Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora;
Bovidae;
OC      Caprinae; Ovis.
XX
RN      [1]
RP      1-238
RA      Md Isa N.;
RT      ;
RL      Submitted (03-FEB-2015) to the INSDC.
RL      College of Medical, Veterinary and Life Sciences, , University of
Glasgow,
RL      Gene and Protein Laboratory, G611QH, UNITED KINGDOM.
XX
RT      "Variation in the sheep MHC-DQB1 locus";
RL      Unpublished.
XX
DR      MD5; 80891213feb5a1b54a983c88828afe66.
XX
FH      Key          Location/Qualifiers
FH
FT      source          1..238
FT          /organism="Ovis aries"
FT          /mol_type="genomic DNA"
FT          /PCR_primers="fwd_name: JM05, fwd_seq:
FT          tccccgcagaggatttcgtg, rev_name: JM06, rev_seq:

```



```

FT          ctcgccgctgccagggtgaagg"
FT          /db_xref="taxon:9940"
FT  CDS      <1..>238
FT          /codon_start=1
FT          /transl_table=1
FT          /gene="DQB1"
FT          /allele="DQB1*9t027"
FT          /product="MHC class II antigen"
FT          /function="antigen presenting molecule"
FT          /db_xref="GOA:A0A0D6E2D2"
FT          /db_xref="InterPro:IPR000353"
FT          /db_xref="InterPro:IPR011162"
FT          /db_xref="InterPro:IPR014745"
FT          /db_xref="UniProtKB/TrEMBL:A0A0D6E2D2"
FT          /protein_id="CEP13147.1"
FT
FT          /translation="VQLKGLCYFTNGTERVRLVTRYIYNRQEDVRFDSWDWGEYRGVTPL
FT          GRRQAEYWNSQKDILEQTRAEVDTVCRNNYQVDA"
FT  exon     1..238
FT          /gene="DQB1"
FT          /allele="DQB1*9t027"
FT          /number=2
XX
SQ  Sequence 238 BP; 55 A; 65 C; 86 G; 32 T; 0 other;
gtccaggttaa agggcctgtg ttacttcacc aacgggacgg agcgggtgcg gctcgtgacc
60
agatacatct acaaccggca agaggacgtg cgcttcgaca gcgactgggg cgagtaccgc
120
gggggtgaccc cgctggggcg gcggcaagcc gagtactgga acagccagaa ggacatcctg
180
gagcagacgc gggccgaggt ggacacggtg tgcagaaaca actaccaggt ggatgccc
238
//
ID  LN868258; SV 1; linear; genomic DNA; STD; MAM; 367 BP.
XX
AC  LN868258;
XX
DT  01-JUL-2015 (Rel. 125, Created)
DT  01-JUL-2015 (Rel. 125, Last updated, Version 1)
XX
DE  Ovis aries partial Ovar-DQB1 gene for MHC class II antigen, breed
Texel,
DE  isolate 8t013, allele Ovar-DQB1*8t013, exon 2
XX
KW  .
XX
OS  Ovis aries (sheep)
OC  Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia;
OC  Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora;
Bovidae;
OC  Caprinae; Ovis.
XX
RN  [1]
RP  1-367
RA  Md Isa N.;
RT  ;
RL  Submitted (10-JUN-2015) to the INSDC.
RL  College of Medical, Veterinary and Life Sciences, University of
Glasgow,
RL  Gene and Protein Laboratory, G611QH, UNITED KINGDOM.
RT  "Variation in the sheep MHC-DQB1 locus";
RL  Unpublished.

```

```

XX
DR   MD5; 71ba8136b8b1f6abc3bf73dd939b5af9.
XX
FH   Key                      Location/Qualifiers
FH
FT   source                    1..367
FT                               /organism="Ovis aries"
FT                               /isolate="8t013"
FT                               /mol_type="genomic DNA"
FT                               /PCR_primers="fwd_name: 991, fwd_seq:
ctgaccgagcggctgt,
FT                               rev_name: 994, rev_seq: cggctctctgtcccatcc"
FT                               /note="Breed:Texel"
FT                               /db_xref="taxon:9940"
FT   CDS                       <13..>279
FT                               /codon_start=1
FT                               /transl_table=1
FT                               /gene="Ovar-DQB1"
FT                               /allele="Ovar-DQB1*8t013"
FT                               /product="MHC class II antigen"
FT                               /function="antigen presenting molecule"
FT                               /protein_id="CRX76979.1"
FT
/translation="DFVVQFKGLCYFTNGTERVRHVTRYIYNQEEYARFSDSDWDEYRAV
FT                               TPLGRPD AEYWNSQEDILEQTRAEADTVCRHNYQNELITSLQRR"
FT   exon                      13..279
FT                               /gene="Ovar-DQB1"
FT                               /allele="Ovar-DQB1*8t013"
FT                               /number=2
XX
SQ   Sequence 367 BP; 72 A; 118 C; 128 G; 49 T; 0 other;
60   ctccccgcag aggatttcgt ggtccagttt aagggcctgt gttacttcac caacgggacg
120   gagcgggtgc ggcattgtgac cagatacatc tacaaccagg aggagtacgc gcgcttcgac
180   agcgactggg acgagtaccg ggcgggtgacg ccgctggggc ggccggacgc cgagtactgg
240   aacagccagg aggacatcct ggagcagacg cgggccgagg cggacacggt gtgcagacac
300   aactaccaga acgaactcat cacatccttg cagcggcgag gtgagtgccg gccgccctcc
360   gcgggggcgc cctccaccct ccgcgcggga gggactgagt cctccggggc ggggtcccca
367   gaccac
//
ID   LN868259; SV 1; linear; genomic DNA; STD; MAM; 377 BP.
XX
AC   LN868259;
XX
DT   01-JUL-2015 (Rel. 125, Created)
DT   01-JUL-2015 (Rel. 125, Last updated, Version 1)
XX
DE   Ovis aries partial Ovar-DQB1 gene for MHC class II antigen, breed
Texel,
DE   isolate 8t023, allele Ovar-DQB1*8t023, exon 2
XX
KW   .
XX
OS   Ovis aries (sheep)
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia;

```

OC Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora;
 Bovidae;
 OC Caprinae; Ovis.
 XX
 RN [1]
 RP 1-377
 RA Md Isa N.;
 RT ;
 RL Submitted (10-JUN-2015) to the INSDC.
 RL College of Medical, Veterinary and Life Sciences, University of
 Glasgow,
 RL Gene and Protein Laboratory, G611QH, UNITED KINGDOM.
 RT "Variation in the sheep MHC-DQB1 locus";
 RL Unpublished.
 XX
 DR MD5; fe8c58ce26f1b99c1e00a8783ca13ea0.
 XX
 FH Key Location/Qualifiers
 FH
 FT source 1..377
 FT /organism="Ovis aries"
 FT /isolate="8t023"
 FT /mol_type="genomic DNA"
 FT /PCR_primers="fwd_name: 991, fwd_seq:
 ctgaccgagcggtgt,
 FT rev_name: 994, rev_seq: cggctctctgtcccatcc"
 FT /note="Breed:Texel"
 FT /db_xref="taxon:9940"
 FT CDS <13..>279
 FT /codon_start=1
 FT /transl_table=1
 FT /gene="Ovar-DQB1"
 FT /allele="Ovar-DQB1*8t023"
 FT /product="MHC class II antigen"
 FT /function="antigen presenting molecule"
 FT /protein_id="CRX76980.1"
 FT
 /translation="DFVYQFICHCYFTNGTERVRYVTRYIYNQEEFVRFDSWDWEHRAV
 FT TPLGRPD AEYWN SQKDILERTAEVDTVCRNNYQGELLTSLQRR"
 FT exon 13..279
 FT /gene="Ovar-DQB1"
 FT /allele="Ovar-DQB1*8t023"
 FT /number=2
 XX
 SQ Sequence 377 BP; 72 A; 121 C; 130 G; 54 T; 0 other;
 ctccccgcag aggatttcgt gtaccagttt atatgccact gttacttcac caacgggacg
 60
 gagcgggtgc ggtacgtgac cagatacatc tacaaccagg aagagtctgt gcgcttcgac
 120
 agcgactggg acgagcaccg ggcgggtgacg ccgctggggc ggccggacgc cgagtactgg
 180
 aacagccaga aggacatcct ggagcggacg cgggccgagg tggacacggt gtgcagaaac
 240
 aactaccagg gggagctcct cacctccttg cagcggcgag gtgagtgccg gccgcctcc
 300
 gcgtgctcgc cctccacccg ccaggactcc gcgcggggag ggggctgagt cctccagggc
 360
 ggggtcccca gaccac
 377
 //

ID LN868260; SV 1; linear; genomic DNA; STD; MAM; 367 BP.
 XX

AC LN868260;
XX
DT 01-JUL-2015 (Rel. 125, Created)
DT 01-JUL-2015 (Rel. 125, Last updated, Version 1)
XX
DE Ovis aries partial Ovar-DQB1 gene for MHC class II antigen, breed
Texel,
DE isolate 0t041, allele Ovar-DQB1*0t041, exon 2
XX
KW .
XX
OS Ovis aries (sheep)
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia;
OC Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora;
Bovidae;
OC Caprinae; Ovis.
XX
RN [1]
RP 1-367
RA Md Isa N.;
RT ;
RL Submitted (10-JUN-2015) to the INSDC.
RL College of Medical, Veterinary and Life Sciences, University of
Glasgow,
RL Gene and Protein Laboratory, G611QH, UNITED KINGDOM.
RT "Variation in the sheep MHC-DQB1 locus";
RL Unpublished.
XX
DR MD5; 8540e8602e6db46053d7500b3b107a0a.
XX
FH Key Location/Qualifiers
FH
FT source 1..367
FT /organism="Ovis aries"
FT /isolate="0t041"
FT /mol_type="genomic DNA"
FT /PCR_primers="fwd_name: 991, fwd_seq:
ctgaccgagcggctgt,
FT rev_name: 994, rev_seq: cggctctctgtcccatcc"
FT /note="Breed:Texel"
FT /db_xref="taxon:9940"
FT CDS <13..>279
FT /transl_table=1
FT /gene="Ovar-DQB1"
FT /allele="Ovar-DQB1*0t041"
FT /product="MHC class II antigen"
FT /function="antigen presenting molecule"
FT /protein_id="CRX76981.1"
FT
/translation="DFVVQFKGLCYFTNGTERVRLVTRYIYNQEEYARFDSWDEYRAV
FT TPLGRPD AEYWNSQEDILEQTRAEADTVCRHNYQNELITSLQRR"
FT exon 13..279
FT /gene="Ovar-DQB1"
FT /allele="Ovar-DQB1*0t041"
FT /number=2
XX
SQ Sequence 367 BP; 72 A; 119 C; 127 G; 49 T; 0 other;
ctccccgcag aggatttcgt ggtccagttt aagggcctgt gttacttcac caacgggaca
60
gagcgggtgc ggctcgtgac cagatacatc tacaaccagg aggagtacgc gcgcttcgac
120

```

    agcgactggg acgagtaccg ggcggtgacg ccgctggggc ggccggacgc cgagtactgg
180
    aacagccagg aggacatcct ggagcagacg cgggccgagg cggacacggt gtgcagacac
240
    aactaccaga acgaactcat cacatccttg cagcggcgag gtgagtgccg gccgccctcc
300
    gcgggggcgc cctccaccct ccgcgcggga gggactgagt cctccggggc ggggtcccca
360
    gaccac
367
//ID    LN868261; SV 1; linear; genomic DNA; STD; MAM; 375 BP.
XX
AC    LN868261;
XX
DT    01-JUL-2015 (Rel. 125, Created)
DT    01-JUL-2015 (Rel. 125, Last updated, Version 1)
XX
DE    Ovis aries partial Ovar-DQB1 gene for MHC class II antigen, breed
Texel,
DE    isolate 0t175, allele Ovar-DQB1*0t175, exon 2
XX
KW    .
XX
OS    Ovis aries (sheep)
OC    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia;
OC    Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora;
Bovidae;
OC    Caprinae; Ovis.
XX
RN    [1]
RP    1-375
RA    Md Isa N.;
RT    ;
RL    Submitted (10-JUN-2015) to the INSDC.
RL    College of Medical, Veterinary and Life Sciences, University of
Glasgow,
RL    Gene and Protein Laboratory, G611QH, UNITED KINGDOM.
RT    "Variation in the sheep MHC-DQB1 locus";
RL    Unpublished.
XX
DR    MD5; a75f112686f92dc797440ef25194cea5.
XX
FH    Key          Location/Qualifiers
FH
FT    source          1..375
FT                    /organism="Ovis aries"
FT                    /isolate="0t175"
FT                    /mol_type="genomic DNA"
FT                    /PCR_primers="fwd_name: 991, fwd_seq:
ctgaccgagcggctgt,
FT                    rev_name: 994, rev_seq: cggctctctgtcccatcc"
FT                    /note="Breed:Texel"
FT                    /db_xref="taxon:9940"
FT    CDS              <13..>279
FT                    /transl_table=1
FT                    /gene="Ovar-DQB1"
FT                    /allele="Ovar-DQB1*0t175"
FT                    /product="MHC class II antigen"
FT                    /function="antigen presenting molecule"
FT                    /protein_id="CRX76982.1"
FT
/translation="DFVYQFKGLCYFTNGTERVRLVTRYIYNQEEYVRFDSDWDEYRAV

```

FT TPLGRRSAEYWNSQKDILEQTRAAVDTVCRHNYQNELITSLQRR"
 FT exon 13..279
 FT /gene="Ovar-DQB1"
 FT /allele="Ovar-DQB1*0t175"
 FT /number=2
 XX
 SQ Sequence 375 BP; 73 A; 120 C; 130 G; 52 T; 0 other;
 ctccccgcag aggatttcgt gtaccagttt aagggcctgt gttacttcac caacgggacg
 60 gagcgggtgc ggctcgtgac cagatacatc tacaaccagg aggagtacgt gcgcttcgac
 120 agcgactggg acgagtaccg ggcggtgacc ccgctggggc ggcgagcgcg cgagtactgg
 180 aacagccaga aggacatcct ggagcagacg cgggccgcgg tggacacggt gtgcagacac
 240 aactaccaga acgagctcat cacatccttg cagcggcgag gtgagtgccg gccgccctcc
 300 gcggggccgc ccttcacccg ccaggactcc gcgcaggagg ggctgagtcc tccggggcgg
 360 ggtccccaga cccac
 375
 //
 ID LN868264; SV 1; linear; genomic DNA; STD; MAM; 377 BP.
 XX
 AC LN868264;
 XX
 DT 01-JUL-2015 (Rel. 125, Created)
 DT 01-JUL-2015 (Rel. 125, Last updated, Version 1)
 XX
 DE Ovis aries partial Ovar-DQB1 gene for MHC class II antigen, breed
 Texel,
 DE isolate 8t006, allele Ovar-DQB1*8t006, exon 2
 XX
 KW .
 XX
 OS Ovis aries (sheep)
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia;
 OC Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia; Pecora;
 Bovidae;
 OC Caprinae; Ovis.
 XX
 RN [1]
 RP 1-377
 RA Md Isa N.;
 RT ;
 RL Submitted (11-JUN-2015) to the INSDC.
 RL College of Medical, Veterinary and Life Sciences, University of
 Glasgow,
 RL Gene and Protein Laboratory, G611QH, UNITED KINGDOM.
 RT "Variation in the sheep MHC-DQB1 locus";
 RL Unpublished.
 XX
 DR MD5; fd0b0973da554d808959396fbd0675b6.
 XX
 FH Key Location/Qualifiers
 FH
 FT source 1..377
 FT /organism="Ovis aries"
 FT /isolate="8t006"
 FT /mol_type="genomic DNA"
 FT /PCR_primers="fwd_name: 991, fwd_seq:
 ctgaccgagcggctgt,

```

FT          rev_name: 994, rev_seq: cggctctctgtcccatcc"
FT          /note="Breed:Texel"
FT          /db_xref="taxon:9940"
FT  CDS      <12..>279
FT          /codon_start=1
FT          /transl_table=1
FT          /gene="Ovar-DQB1"
FT          /allele="Ovar-DQB1*8t006"
FT          /product="MHC class II antigen"
FT          /function="antigen presenting molecule"
FT          /protein_id="CRX76985.1"
FT
FT          /translation="GFRVPAYRPFVLLHQRDGAGAARDQIHLQPGRVRALRQRLGRVPGG
FT          DAAGAAVRRVLEQPEGHPGADAGRGGHGVQKQLPGGAPHLLAAA"
FT  exon      12..279
FT          /gene="Ovar-DQB1"
FT          /allele="Ovar-DQB1*8t006"
FT          /number=2
XX
SQ  Sequence 377 BP; 70 A; 122 C; 131 G; 54 T; 0 other;
      ctccccgcag aggatttcgt gtaccagctt ataggccagt gttacttcac caacgggacg
60
      gagcgggtgc ggctcgtgac cagatacatc tacaaccagg aagagttcgt gcgcttcgac
120
      agcgactggg acgagtaccg ggcgggtgacg ccgctggggc ggccgtccgc cgagtactgg
180
      aacagccaga aggacatcct ggagcggacg cgggccgagg tggacacggt gtgcagaaac
240
      aactaccagg gggagctcct cacctccttg cagcggcgag gtgagtgccg gccgccctcc
300
      gcgtgctcgc cctccacccg ccaggactcc gcgcggggag ggggctgagt cctccagggc
360
      ggggtcccca gaccac
377
//

```

Appendix 6: Amino Acid Abbreviation

Local name	Accession number	IPD name
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn	N
Aspartic acid	Asp	D
Cysteine	Cys	C
Glutamine	Gln	Q
Glutamic acid	Glu	E
Glycine	Gly	G
Histidine	His	H
Isoleucine	Ile	I
Leucine	Leu	L
Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V

Appendix 7: SAS Commands

Filename bbmhc dde

'Excel|J:\Vet\Teladorsagia\Texelmjs\JOanalyses\[texBBhaplos2.xls]sheet1!R6C1:
R242C15';

```
data bblafmhc;

  infile bbmhc missover;

  input lamb $ familyid $ sire $ siredrb1a $ siredrb1b $ dam $ damdrb1a $
damdrb1b $

  drb1a $ drb1b $ source $ csrd226a $ csrd226b $ omhc1a $ omhc1b $;

  **if drb1a = '*' then delete;

  drop source;

  if drb1b = '*' then drb1b = drb1a;

  if drb1a = '0' then drb1a = ' ';

  if drb1b = '0' then drb1b = ' ';

  if csrd226a = '0' then csrd226a = ' ';

  if csrd226b = '0' then csrd226b = ' ';

  if omhc1a = '0' then omhc1a = ' ';

  if omhc1b = '0' then omhc1b = ' ';

  if lamb = ' ' then lamb = ' ';

  if sire = ' ' then sire = ' ';

  if dam = ' ' then dam = ' ';

  if drb1a = ' ' then drb1a = ' ';

  if drb1b = ' ' then drb1b = ' ';

  if csrd226a = ' ' then csrd226a = ' ';

  if csrd226b = ' ' then csrd226b = ' ';

  if omhc1a = ' ' then omhc1a = ' ';
```

if omhc1b = ' ' then omhc1b = ' ';

typed by Nicola;

if lamb = '098t052' then drb1a = 'M';

if lamb = '098t052' then drb1b = 'M';

if lamb = '098t057' then drb1a = 'M';

if lamb = '098t057' then drb1b = 'H3';

if lamb = '098t060' then drb1a = ' ';

if lamb = '098t060' then drb1b = ' ';

if lamb = '098t063' then drb1a = ' ';

if lamb = '098t063' then drb1b = ' ';

typed by Nicola;

if lamb = '098t074' then drb1a = 'M';

if lamb = '098t074' then drb1b = 'H3';

if lamb = '099t005' then drb1a = 'L';

if lamb = '099t005' then drb1b = 'A';

if lamb = '099t019' then drb1a = ' ';

if lamb = '099t019' then drb1b = ' ';

**if lamb = '099t027' then drb1a = ' ';

**if lamb = '099t027' then drb1b = ' ';

typed by Nicola;

if lamb = '099t031' then drb1a = 'G2';

if lamb = '099t031' then drb1b = 'FN543114 ';

if lamb = '099t056' then drb1a = ' ';

if lamb = '099t056' then drb1b = ' ';

typed by Nicola;

if lamb = '099t074' then drb1a = 'M';

if lamb = '099t074' then drb1b = 'G2';

typed by Nicola;

```

if lamb = '099t078' then drb1a = 'G2';
if lamb = '099t078' then drb1b = 'M';
***if lamb = '099t079' then drb1a = ' ';
***if lamb = '099t079' then drb1b = ' ';
***typed by Nicola***;

if lamb = '099t082' then drb1a = 'H3';
if lamb = '099t082' then drb1b = 'M';
if lamb = '099t087' then drb1a = ' ';
if lamb = '099t087' then drb1b = ' ';
***typed by Nicola***;

if lamb = '099t094' then drb1a = 'M';
if lamb = '099t094' then drb1b = 'H3';
if lamb = '099t097' then drb1a = ' ';
if lamb = '099t097' then drb1b = ' ';
***typed by Nicola***;

if lamb = '100t013' then drb1a = 'M';
if lamb = '100t013' then drb1b = 'HG515541';
if lamb = '100t020' then drb1a = 'D2 ';
if lamb = '100t020' then drb1b = 'A';
if lamb = '100t046' then drb1a = 'GSF';
if lamb = '100t046' then drb1b = 'G2';
if lamb = '100t053' then drb1a = 'D2';
if lamb = '100t053' then drb1b = 'FN393738';
if lamb = '100t062' then drb1a = 'H3';
if lamb = '100t062' then drb1b = 'G2';
if lamb = '100t063' then drb1a = ' ';
if lamb = '100t063' then drb1b = ' ';
if lamb = '100t067' then drb1a = ' ';
if lamb = '100t067' then drb1b = ' ';

```

```

if lamb = '100t068' then drb1a = ' ';
if lamb = '100t068' then drb1b = ' ';
***typed by Nicola***;
if lamb = '100t080' then drb1a = 'D2';
if lamb = '100t080' then drb1b = 'M';
if lamb = '100t085' then drb1a = ' ';
if lamb = '100t085' then drb1b = ' ';
***typed by Nicola***;
if lamb = '100t097' then drb1a = 'D2';
if lamb = '100t097' then drb1b = 'FM998807';
***typed by Nicola***;
if lamb = '100t104' then drb1a = 'A';
if lamb = '100t104' then drb1b = 'H3';
if lamb = '100t129' then delete;
if lamb = '100t129' then delete;
***typed by Nicola***;
if lamb = '100t137' then drb1a = 'GSF';
if lamb = '100t137' then drb1b = 'TUV';
if lamb = '100t142' then drb1a = ' ';
if lamb = '100t142' then drb1b = ' ';
if lamb = '100t166' then drb1a = ' ';
if lamb = '100t166' then drb1b = ' ';
***typed by Nicola***;
if lamb = '100t167' then drb1a = 'H3';
if lamb = '100t167' then drb1b = 'M';

keep lamb sire dam drb1a drb1b csrd226a csrd226b omhc1a omhc1b;

**file 'J:\VET\Teladorsagia\Texelmjs\JOanalyses\texelmhc.dat';

**put @1 lamb @10 sire @17 dam @24 drb1a @31 drb1b @38 csrd226a @45
csrd226b @52 omhc1a @59

```

```
omhc1b;
```

```
run;
```

```
proc sort;
```

```
by lamb;
```

```
run;
```

```
Filename bbDQA1 dde
```

```
'Excel|J:\Vet\Teladorsagia\Texelmjs\JOanalyses\[Texeldqa1ds.xls]DQA1!R2C1:R353C3';
```

```
data DQA1;
```

```
infile bbDQA1 missover;
```

```
input lamb $ dqa1a $ dqa1b $;
```

```
if dqa1a = '.' then if dqa1b = '.' then delete;
```

```
if dqa1a = 'x' then dqa1a = 'Null';
```

```
if dqa1b = 'x' then dqa1b = 'Null';
```

```
if dqa1a = '.' then dqa1a = ' ';
```

```
if dqa1b = '.' then dqa1b = ' ';
```

```
if dqa1a = 'Z28420' then dqa1a = '92.y085';
```

```
if dqa1b = 'Z28420' then dqa1b = '92.y085';
```

```
if dqa1a = 'AF276954' then dqa1a = 'HE574809';
```

```
if dqa1b = 'AF276954' then dqa1b = 'HE574809';
```

```
if lamb = '099t005' then dqa1a = ' ';
```

```
if lamb = '099t005' then dqa1b = ' ';
```

```
if lamb = '099t027' then dqa1a = ' ';
```

```
if lamb = '099t027' then dqa1b = ' ';
```

```
if lamb = '099t083' then dqa1a = ' ';
```

```
if lamb = '099t083' then dqa1b = ' ';
```

```

***if lamb = '100t053' then dqa1a = ' ';
***if lamb = '100t053' then dqa1b = ' ' updated;

if lamb = '100t149' then dqa1a = ' ';
if lamb = '100t149' then dqa1b = ' ';

run;

```

```

proc sort;

  by lamb;

run;

```

```
filename bbdqb1 dde
```

```
'Excel|J:\Vet\Teladorsagia\Texelmjs\JOanalyses\[COMPLETE
TEXEL.XLS]Sheet1!R2C1:R235C6';
```

DQB1-

```

data dqb1;

  infile bbdqb1 missover;

  input lamb $ dna pcr1 $ pcr2 $ dqb1a $ dqb1b $ ;

  if dqb1a = '?' then dqb1a= 'New';
  if dqb1b = '?' then dqb1b= 'New';

  if dqb1b= 'N' then dqb1b = '.';
  if dqb1a= 'N' then dqb1a = '.';
  if dqb1a = ' ' then dqb1a = '.';
  if dqb1b = ' ' then dqb1b = '.';
  if dqb1a = 'X' then dqb1a = '.';
  if dqb1b = 'X' then dqb1b = '.';
  if dqb1a = 'x' then dqb1a = '.';
  if dqb1b = 'x' then dqb1b = '.';
  if dqb1a = 'N' then dqb1a = '.';
  if dqb1b = 'N' then dqb1a = '.';

```

```

if dqb1a = 'y18' then dqb1a = 'GU191460';
if dqb1b = 'y18' then dqb1b = 'GU191460';
if dqb1a = '13a' then dqb1a = 'GU191460';
if dqb1b = '13a' then dqb1a = 'GU191460';
if dqb1a = 'TNEW1CLONE' then dqb1a = 'GU191455';
if dqb1b = 'TNEW1CLONE' then dqb1b = 'GU191455';
if dqb1a = 'tnew1' then dqb1a = 'GU191455';
if dqb1b = 'tnew1' then dqb1b = 'GU191455';
if dqb1a = 'tnew5' then dqa1a = 'Null';
if dqb1b = 'tnew5' then dqa1b = 'Null';
***if dqb1a = '4389_4' then dqb1a = 'Null';
***if dqb1b = '4389_4' then dqb1b = 'Null';
keep lamb dqb1a dqb1b ;

run;

```

```

proc sort;
  by lamb;
run;

```

Filename bbdqa2 dde

'Excel|K:\Vet\Teladorsagia\Texelmjs\JOanalyses\[Texel_DQA2.XLS]sheet1!R2C1:R234C7';

```

data dqa2;
  infile bbdqa2 missover;

  input lamb $ dna pcr $ dqa2a $ dqa2b $ dqa2likea $ dqa2likeb $;

  if dqa2a = ' ' then dqa2a = '.';
  if dqa2a = '?' then dqa2a = '.';
  if dqa2a = 'N' then dqa2a = '.';

```

```

if dqa2b = ' ' then dqa2b = '.';
if dqa2b = '?' then dqa2b = '.';
if dqa2b = 'N' then dqa2b = '.';
if dqa2a = 'X' then dqa2a = '.';
if dqa2b = 'X' then dqa2b = '.';
if dqa2a = 'badseq' then dqa2a = '.';
if dqa2b = 'badseq' then dqa2b = '.';
if dqa2a = 'REDO' then dqa2a = '.';
if dqa2b = 'REDO' then dqa2b = '.';
if dqa2a = '.' then dqa2a = ' ';
if dqa2b = '.' then dqa2b = ' ';

```

```

keep lamb dqa2a dqa2b dqa2likea dqa2likeb;

```

```

run;

```

```

proc sort;

```

```

by lamb;

```

```

run;

```

Filename DS2 dde

```

'Excel|J:\Vet\Teladorsagia\Texelmjs\JOanalyses\[Texel-MHC-Review-
DS.xls]DQB2!R2C1:R353C3';

```

```

data DQB2;

```

```

infile DS2 missover;

```

```

input lamb $ dqb2a $ dqb2b $;

```

```

if dqb2a = '.' then dqb2a = ' ';

```

```

if dqb2b = '.' then dqb2b = ' ';

```

```

if dqb2a = 'x' then dqb2a = ' ';

```



```

if dqb2b = 'x' then dqb2b = ' ';
***if dqb2a = '.' then if dqb2b = '.' then delete;
run;

```

```

proc sort;

by lamb;

run;

```

Filename DS2R dde

'Excel|J:\Vet\Teladorsagia\Texelmjs\JOanalyses\[MahizaDQB2.xlsx]Sheet1!R2C1:
R231C3';

```

data DQB2r;

infile DS2R missover;

input lamb $ dqb2ar $ dqb2br $;

run;

```

```

proc sort;

by lamb;

run;

```

```

data allmhc;

merge bblafmhc DQA1 DQB1 DQA2 DQB2 DQB2R;

by lamb;

***if lamb = '100t012A' then lamb = '100t012A';

if lamb = '100t012A' then delete;

if lamb = '100t012B' then delete;

***if lamb = '100t073A' then lamb = '100t073';

```

```

***if lamb = '100t073B' then lamb = '100t073';

if lamb = '100t073' then dqa2a = 'AY312382';
if lamb = '100t073' then dqa2b = 'AY312388';
if lamb = '100t073' then dqa2likea = 'Null';
if lamb = '100t073' then dqa2likeb = 'Null';
if lamb = '100t129' then delete;

***if lamb = '100t155A' then lamb = '100t155';
if lamb = '100t155' then dqa2a = 'AY312381';
if lamb = '100t155' then dqa2b = 'AY312382';
if dam = ' ' then delete;

If drb1a = 'DQ659115' then drb1a = '1501';
If drb1b = 'DQ659115' then drb1b = '1501';
If drb1a = '228' then drb1a = 'FR686849';
If drb1b = '228' then drb1b = 'FR686849';
If drb1a = '8t047' then drb1a = 'FN393738';
If drb1b = '8t047' then drb1b = 'FN393738';

***file 'J:\VET\Teladorsagia\Texelmjs\JOanalyses\texelmhc.txt';

***put @1 lamb @9 sire @17 dam @24 drb1a @31 drb1b @35 csrd226a @39
csrd226b @44 omhc1a @49

omhc1b

@53 dqa1a @62 dqa1b @71 dqb1a @80 dqb1b @89 dqa2a @98 dqa2b @107
dqb2a @116 dqb2b;

***if sire = ' ' then delete;

run;

```

Filename	hap	dde
'Excel J:\VET\Teladorsagia\Texelmjs\JOanalyses\[Texel_Haplotypes.xls]DQB2!R2		
C1:R353C3';		

```

data haplo;

infile hap missover;

    input lamb $ shap $ dhap $;

if shap = '1' then shap = '01';
if shap = '2' then shap = '02';
if shap = '3' then shap = '03';
if shap = '4' then shap = '04';
if shap = '5' then shap = '05';
if shap = '6' then shap = '06';
if shap = '7' then shap = '07';
if shap = '8' then shap = '08';
if shap = '9' then shap = '09';
if dhap = '1' then dhap = '01';
if dhap = '2' then dhap = '02';
if dhap = '3' then dhap = '03';
if dhap = '4' then dhap = '04';
if dhap = '5' then dhap = '05';
if dhap = '6' then dhap = '06';
if dhap = '7' then dhap = '07';
if dhap = '8' then dhap = '08';
if dhap = '9' then dhap = '09';
if shap = ' ' then if dhap = ' ' then delete;
if lamb = '100t067' then delete;
if lamb = '100t129' then delete;

run;

proc sort;

    by lamb;

```

```

run;

data shaplo;

set haplo;

hap = shap;

keep lamb hap;


data dhaplo;

set haplo;

hap=dhap;

keep lamb hap;


proc sort;

by lamb hap;


data monohap;

merge shaplo dhaplo;

by lamb hap;

run;


data allhap;

merge allmhc haplo;

by lamb;

***if dhap = '08' then put lamb dhap;

***if dhap = '20' then put lamb dhap;

if shap = '01' then oladrb1a = '0901';

if dhap = '01' then oladrb1b = '0901';

if shap = '02' then oladrb1a = '0601';

if dhap = '02' then oladrb1b = '0601';

if shap = '03' then oladrb1a = '0401';

```

if dhap = '03' then oladrb1b = '0401';
if shap = '04' then oladrb1a = '1601';
if dhap = '04' then oladrb1b = '1601';
if shap = '05' then oladrb1a = '1501';
if dhap = '05' then oladrb1b = '1501';
if shap = '06' then oladrb1a = 'FN393738';
if dhap = '06' then oladrb1b = 'FN393738';
if shap = '07' then oladrb1a = 'FN543114';
if dhap = '07' then oladrb1b = 'FN543114';
if shap = '08' then oladrb1a = 'FN870432';
if dhap = '08' then oladrb1b = 'FN870432';
if shap = '09' then oladrb1a = 'FR686849';
if dhap = '09' then oladrb1b = 'FR686849';
if shap = '10' then oladrb1a = 'FR686849';
if dhap = '10' then oladrb1b = 'FR686849';
if shap = '11a' then oladrb1a = '1101';
if dhap = '11a' then oladrb1b = '1101';
if shap = '11b' then oladrb1a = '1101';
if dhap = '11b' then oladrb1b = '1101';
if shap = '12' then oladrb1a = '1401';
if dhap = '12' then oladrb1b = '1401';
if shap = '13' then oladrb1a = '0102';
if dhap = '13' then oladrb1b = '0102';
if shap = '14' then oladrb1a = 'HQ515541';
if dhap = '14' then oladrb1b = 'HQ515541';
if shap = '15' then oladrb1a = '0302';
if dhap = '15' then oladrb1b = '0302';
if shap = '16' then oladrb1a = '0201';
if dhap = '16' then oladrb1b = '0201';

if shap = '17' then oladrb1a = '0701';
 if dhap = '17' then oladrb1b = '0701';
 if shap = '18' then oladrb1a = 'U00219';
 if dhap = '18' then oladrb1b = 'U00219';
 if shap = '19' then oladrb1a = 'FM998807';
 if dhap = '19' then oladrb1b = 'FM998807';
 if shap = '20' then oladrb1a = '0201';
 if dhap = '20' then oladrb1b = '0201';
 if shap = '01' then oladqa1a = 'LN827891';
 if dhap = '01' then oladqa1b = 'LN827891';
 if shap = '02' then oladqa1a = 'M33304';
 if dhap = '02' then oladqa1b = 'M33304';
 if shap = '03' then oladqa1a = 'LN827894';
 if dhap = '03' then oladqa1b = 'LN827894';
 if shap = '04' then oladqa1a = 'LN827892';
 if dhap = '04' then oladqa1b = 'LN827892';
 if shap = '05' then oladqa1a = 'LN827893';
 if dhap = '05' then oladqa1b = 'LN827893';
 if shap = '06' then oladqa1a = 'LN827890';
 if dhap = '06' then oladqa1b = 'LN827890';
 if shap = '07' then oladqa1a = 'M33304';
 if dhap = '07' then oladqa1b = 'M33304';
 if shap = '08' then oladqa1a = 'LN827891';
 if dhap = '08' then oladqa1b = 'LN827891';
 if shap = '09' then oladqa1a = 'LN736359';
 if dhap = '09' then oladqa1b = 'LN736359';
 if shap = '10' then oladqa1a = 'M33304';
 if dhap = '10' then oladqa1b = 'M33304';
 if shap = '11a' then oladqa1a = 'Null';

```

if dhap = '11a' then oladqa1b = 'Null';
if shap = '11b' then oladqa1a = 'Null';
if dhap = '11b' then oladqa1b = 'Null';
if shap = '12' then oladqa1a = 'LN827890';
if dhap = '12' then oladqa1b = 'LN827890';
if shap = '13' then oladqa1a = 'M33304';
if dhap = '13' then oladqa1b = 'M33304';
if shap = '14' then oladqa1a = 'M33304';
if dhap = '14' then oladqa1b = 'M33304';
if shap = '15' then oladqa1a = 'LN736359';
if dhap = '15' then oladqa1b = 'LN736359';
if shap = '16' then oladqa1a = 'M33304';
if dhap = '16' then oladqa1b = 'M33304';
if shap = '17' then oladqa1a = 'Null';
if dhap = '17' then oladqa1b = 'Null';
if shap = '18' then oladqa1a = 'M33304';
if dhap = '18' then oladqa1b = 'M33304';
if shap = '19' then oladqa1a = 'M33304';
if dhap = '19' then oladqa1b = 'M33304';
if shap = '20' then oladqa1a = 'LN827890';
if dhap = '20' then oladqa1b = 'LN827890';
****DQB1;
if shap = '01' then oladqb1a = 'AJ238939';
if dhap = '01' then oladqb1b = 'AJ238939';
    if shap = '02' then oladqb1a = 'AH001247';
if dhap = '02' then oladqb1b = 'AH001247';
if shap = '03' then oladqb1a = 'Z28423';
if dhap = '03' then oladqb1b = 'Z28423';
if shap = '04' then oladqb1a = 'GU191456';

```

if dhap = '04' then oladqb1b = 'GU191456';
if shap = '05' then oladqb1a = 'LN811403';
if dhap = '05' then oladqb1b = 'LN811403';
if shap = '06' then oladqb1a = 'GU191453';
if dhap = '06' then oladqb1b = 'GU191453';
if shap = '07' then oladqb1a = 'GU191455';
if dhap = '07' then oladqb1b = 'GU191455';
if shap = '08' then oladqb1a = 'GU191455';
if dhap = '08' then oladqb1b = 'GU191455';
if shap = '09' then oladqb1a = 'AJ238945';
if dhap = '09' then oladqb1b = 'AJ238945';
if shap = '10' then oladqb1a = 'HQ728667';
if dhap = '10' then oladqb1b = 'HQ728667';
if shap = '11a' then oladqb1a = 'Null';
if dhap = '11a' then oladqb1b = 'Null';
if shap = '11b' then oladqb1a = 'Null';
if dhap = '11b' then oladqb1b = 'Null';
if shap = '12' then oladqb1a = 'GU191460';
if dhap = '12' then oladqb1b = 'GU191460';
if shap = '13' then oladqb1a = 'HQ728667';
if dhap = '13' then oladqb1b = 'HQ728667';
if shap = '14' then oladqb1a = 'AH001247';
if dhap = '14' then oladqb1b = 'AH001247';
if shap = '15' then oladqb1a = 'AJ238945';
if dhap = '15' then oladqb1b = 'AJ238945';
if shap = '16' then oladqb1a = 'GU191455';
if dhap = '16' then oladqb1b = 'GU191455';
if shap = '17' then oladqb1a = 'LN811404';
if dhap = '17' then oladqb1b = 'LN811404';


```

if shap = '18' then oladqb1a = 'HQ728667';
if dhap = '18' then oladqb1b = 'HQ728667';
if shap = '19' then oladqb1a = 'HQ728667';
if dhap = '19' then oladqb1b = 'HQ728667';
if shap = '20' then oladqb1a = 'GU191457';
if dhap = '20' then oladqb1b = 'GU191457';
****DQA2;
if shap = '01' then oladqa2a = '1001';
if dhap = '01' then oladqa2b = '1001';
    if shap = '02' then oladqa2a = '0103';
if dhap = '02' then oladqa2b = '0103';
if shap = '03' then oladqa2a = '0601';
if dhap = '03' then oladqa2b = '0601';
if shap = '04' then oladqa2a = '0601';
if dhap = '04' then oladqa2b = '0601';
if shap = '05' then oladqa2a = '08012';
if dhap = '05' then oladqa2b = '08012';
if shap = '06' then oladqa2a = '0901';
if dhap = '06' then oladqa2b = '0901';
if shap = '07' then oladqa2a = '0101';
if dhap = '07' then oladqa2b = '0101';
if shap = '08' then oladqa2a = '0602';
if dhap = '08' then oladqa2b = '0602';
if shap = '09' then oladqa2a = '1101';
if dhap = '09' then oladqa2b = '1101';
if shap = '10' then oladqa2a = '0103';
if dhap = '10' then oladqa2b = '0103';
if shap = '11a' then oladqa2a = '0101';
if dhap = '11a' then oladqa2b = '0101';

```

```

if shap = '11b' then oladqa2a = '0101';
if dhap = '11b' then oladqa2b = '0101';
if shap = '12' then oladqa2a = '0901';
if dhap = '12' then oladqa2b = '0901';
if shap = '13' then oladqa2a = '0103';
if dhap = '13' then oladqa2b = '0103';
if shap = '14' then oladqa2a = '0103';
if dhap = '14' then oladqa2b = '0103';
if shap = '15' then oladqa2a = '1101';
if dhap = '15' then oladqa2b = '1101';
if shap = '16' then oladqa2a = '0602';
if dhap = '16' then oladqa2b = '0602';
if shap = '17' then oladqa2a = '0101';
if dhap = '17' then oladqa2b = '0101';
if shap = '18' then oladqa2a = '0103';
if dhap = '18' then oladqa2b = '0103';
if shap = '19' then oladqa2a = '0103';
if dhap = '19' then oladqa2b = '0103';
if shap = '20' then oladqa2a = '0901';
if dhap = '20' then oladqa2b = '0901';

```

****DQA2-like;

```

if shap = '01' then oladqa2la = 'Null';
if dhap = '01' then oladqa2lb = 'Null';
    if shap = '02' then oladqa2la = 'Null';
if dhap = '02' then oladqa2lb = 'Null';
if shap = '03' then oladqa2la = 'Null';
if dhap = '03' then oladqa2lb = 'Null';
if shap = '04' then oladqa2la = 'Null';

```

if dhap = '04' then oladqa2lb = 'Null';
if shap = '05' then oladqa2la = 'Null';
if dhap = '05' then oladqa2lb = 'Null';
if shap = '06' then oladqa2la = 'Null';
if dhap = '06' then oladqa2lb = 'Null';
if shap = '07' then oladqa2la = '1401';
if dhap = '07' then oladqa2lb = '1401';
if shap = '08' then oladqa2la = 'Null';
if dhap = '08' then oladqa2lb = 'Null';
if shap = '09' then oladqa2la = 'Null';
if dhap = '09' then oladqa2lb = 'Null';
if shap = '10' then oladqa2la = 'Null';
if dhap = '10' then oladqa2lb = 'Null';
if shap = '11a' then oladqa2la = '1401';
if dhap = '11a' then oladqa2lb = '1401';
if shap = '11b' then oladqa2la = '1401';
if dhap = '11b' then oladqa2lb = '1401';
if shap = '12' then oladqa2la = 'Null';
if dhap = '12' then oladqa2lb = 'Null';
if shap = '13' then oladqa2la = 'Null';
if dhap = '13' then oladqa2lb = 'Null';
if shap = '14' then oladqa2la = 'Null';
if dhap = '14' then oladqa2lb = 'Null';
if shap = '15' then oladqa2la = 'Null';
if dhap = '15' then oladqa2lb = 'Null';
if shap = '16' then oladqa2la = 'Null';
if dhap = '16' then oladqa2lb = 'Null';
if shap = '17' then oladqa2la = '1401';
if dhap = '17' then oladqa2lb = '1401';

if shap = '18' then oladqa2la = 'Null';
if dhap = '18' then oladqa2lb = 'Null';
if shap = '19' then oladqa2la = 'Null';
if dhap = '19' then oladqa2lb = 'Null';
if shap = '20' then oladqa2la = 'Null';
if dhap = '20' then oladqa2lb = 'Null';

****DQB2;

if shap = '01' then oladqb2a = 'LN868261';
if dhap = '01' then oladqb2b = 'LN868261';
if shap = '02' then oladqb2a = 'AJ238935';
if dhap = '02' then oladqb2b = 'AJ238935';
if shap = '03' then oladqb2a = 'GU191459';
if dhap = '03' then oladqb2b = 'GU191459';
if shap = '04' then oladqb2a = 'LN828260';
if dhap = '04' then oladqb2b = 'LN828260';
if shap = '05' then oladqb2a = 'U07032';
if dhap = '05' then oladqb2b = 'U07032';
if shap = '06' then oladqb2a = 'HM367630';
if dhap = '06' then oladqb2b = 'HM367630';
if shap = '07' then oladqb2a = 'U07033';
if dhap = '07' then oladqb2b = 'U07033';
if shap = '08' then oladqb2a = 'Z28424';
if dhap = '08' then oladqb2b = 'Z28424';
if shap = '09' then oladqb2a = 'LN868258';
if dhap = '09' then oladqb2b = 'LN868258';
if shap = '10' then oladqb2a = 'LN868258';
if dhap = '10' then oladqb2b = 'LN868258';
if shap = '11a' then oladqb2a = 'AJ238935';

```

if dhap = '11a' then oladqb2b = 'AJ238935';
if shap = '11b' then oladqb2a = 'AJ238946';
if dhap = '11b' then oladqb2b = 'AJ238946';
if shap = '12' then oladqb2a = 'HM367631';
if dhap = '12' then oladqb2b = 'HM367631';
if shap = '13' then oladqb2a = 'LN868259';
if dhap = '13' then oladqb2b = 'LN868259';
if shap = '14' then oladqb2a = 'LN868264';
if dhap = '14' then oladqb2b = 'LN868264';
if shap = '15' then oladqb2a = 'LN868258';
if dhap = '15' then oladqb2b = 'LN868258';
if shap = '16' then oladqb2a = 'Null';
if dhap = '16' then oladqb2b = 'Null';
if shap = '17' then oladqb2a = 'AJ238943';
if dhap = '17' then oladqb2b = 'AJ238943';
if shap = '18' then oladqb2a = 'LN868259';
if dhap = '18' then oladqb2b = 'LN868259';
if shap = '19' then oladqb2a = 'LN868259';
if dhap = '19' then oladqb2b = 'LN868259';
if shap = '20' then oladqb1a = 'AJ238934';
if dhap = '20' then oladqb2b = 'AJ238934';

run;

proc sort data=allhap;
by lamb;
run;

proc print data=allhap;

```

```

    var lamb sire dam shap drb1a dqa1a dqb1a dqa2a dqa2likea dqb2a dhap drb1b
    dqa1b dqb1b dqa2b dqa2likeb dqb2b;

        run;

/*

proc sort data=allhap;

    by sire;

    run;

proc print data=allhap;

    var lamb sire dam shap drb1a dqa1a dqb1a dqa2a dqa2likea dqb2a dhap drb1b
    dqa1b dqb1b dqa2b dqa2likeb dqb2b;

        run;

proc sort data=allhap;

    by shap;

    run;

proc print data=allhap;

    var lamb sire dam shap drb1a dqa1a dqb1a dqa2a dqa2likea dqb2a dhap drb1b
    dqa1b dqb1b dqa2b dqa2likeb dqb2b;

        run;

*/

proc sort data=allhap;

    by dhap;

    run;

proc print data=allhap;

    var lamb sire dam shap drb1a dqa1a dqb1a dqa2a dqa2likea dqb2a dhap drb1b
    dqa1b dqb1b dqa2b dqa2likeb dqb2b;

        run;

```

```

/*
proc sort data=allhap;

by dhap;

run;

proc print data=allhap;

var lamb sire dam shap drb1a dqa1a dqb1a dqa2a dqa2likea dqb2a dhap drb1b
dqa1b dqb1b dqa2b dqa2likeb dqb2b;

run;

/*

proc sort data=allhap;

by dam;

run;

proc print data=allhap;

var lamb sire shap drb1a dqa1a dqb1a dqa2a dqa2likea dqb2a dam dhap drb1b
dqa1b dqb1b dqa2b dqa2likeb dqb2b;

run;

proc sort data=allhap;

by lamb;

run;

PROC PRINT DATA=allmhc;

var lamb dqb2a dqb2b dqb2ar dqb2br;

run;

*/

/*

proc sort;

```

```

by dam;

run;

proc print;

    var lamb sire dam drb1a dqa1a dqb1a dqa2a dqa2likea dqb2a drb1b dqa1b
    dqb1b dqa2b dqa2likeb dqb2b;

    run;

proc sort data=allmhc;

by sire lamb;

run;

proc print data=allmhc;

    var lamb sire dam drb1a dqa1a dqb1a dqa2a dqa2likea dqb2a drb1b dqa1b dqb1b
    dqa2b dqa2likeb dqb2b;

    run;

    */

/*

proc sort data=allmhc;

    by drb1a dqa1a dqb1a dqa2a ;

    run;

proc print data=allmhc;

    var lamb sire dam drb1a dqa1a dqb1a dqa2a dqb2ar drb1b dqa1b dqb1b dqa2b
    dqb2br;

    run;

    */

/*

proc sort data=allmhc;

    by drb1b dqa1b dqa2b;

```



```

run;

proc print data=allmhc;

    var lamb sire dam drb1a dqa1a dqb1a dqa2a dqa2likea dqb2a drb1b dqa1b dqb1b
    dqa2b dqa2likeb dqb2b;

run;


proc sort;

    by lamb;

run;


proc print data=allmhc;

    var lamb dqb2a dqb2b dqb2ar dqb2br;

run;

    */
/*

proc sort data=allmhc;

    by drb1b;

run;

proc print;

    var lamb sire dam drb1a dqa1a dqa2a drb1b dqa1b dqa2b;

run;

    */
/*

proc sort data=allmhc;

    by lamb;

run;

proc print;

    var lamb sire dam drb1a drb1b csrd226a csrd226b omhc1a omhc1b dqa1a dqa1b
    dqb1a dqb1b dqa2a

```

```

dqa2b dqb2a dqb2b;

run;

*/

proc allele data=allhap outstat=ld prefix=Marker haplo=given corrcoeff

hmin = 0.01 gmin = 0.5 exact = 10000 boot=1000 seed=123;

var shap dhap oladrb1a oladrb1b oladqa1a oladqa1b oladqb1a oladqb1b
oladqa2a oladqa2b oladqa2la oladqa2lb oladqb2a oladqb2b;

run;

/*

proc allele data=allmhc outstat=ld prefix=Marker haplo=given corrcoeff

hmin = 0.01 gmin = 0.5 exact = 10000 boot=1000 seed=123;

var drb1a drb1b dqa1a dqa1b dqa2a dqa2b dqb1a dqb1b dqb2a dqb2b;

run;

*/

/*

proc haplotype data=allmhc ld se=jackknife maxiter=20 itprint nlag=4 cutoff=0.01;

var drb1a drb1b dqa1a dqa1b dqb1a dqb1b dqa2a dqa2b;

run;

*/

/*

Filename jjp dde

'Excel|J:\Research
Groups\Teladorsagia\Texelmjs\JOanalyses\[Texeligaigejjp.xls]sheet1!R10C3:R23
1C7';

data jjpab;

infile jjp missover;

input lamb $ igel3 igel4 iga13 iga14;

if igel3 < 0 then igel3 = 0;

```

```

if igel4 < 0 then igel4 = 0;
if igoal3 < 0 then igoal3 = 0;
if igoal4 < 0 then igoal4 = 0;
ligel3 = log(igel3+1);
ligel4 = log(igel4+1);
ligoal3 = log(igoal3+1);
ligoal4 = log(igoal4+1);
igel3g=igel3+0.001;
igel4g=igel4+0.001;
igoal3g=igoal3+0.001;
igoal4g=igoal4+0.001;
tigel3 = (igel3g)**0.25;
tigel4 = (igel4g)**0.25;
ligoal3=log10(igoal3g);
ligoal4=log10(igoal4g);
run;

```

```

proc sort;
by lamb;
run;

```

Filename tweight dde

```

'Excel\J:\Research
Groups\Teladorsagia\Texelmjs\JOanalyses\[BBtexallrevmjs.xls]sheet1!R2C1:R422
C25';

```

```

data weight;

```

```

infile tweight missover;

```

```

input lamb $ sire $ dam $ dnum sgroup dgroup littern week year sex dob dage
litters w20 muscle fat

```

```

stjul nmjul staug nmaug stsep nmsep wgt16 wgt20 wgt24;
if stjul = -1 then stjul = .;
    lepgjul = log10(stjul+25);
if staug = -1 then staug = .;
    lepgaug = log10(staug+25);
if stsep = -1 then stsep = .;
    lepgsep = log10(stsep+25);
    logepg = (sum(lepgjul,lepgaug,lepgsep))/3;
if wgt16 = -1 then wgt16 = .;
if wgt20 = -1 then wgt20 = .;
if wgt24 = -1 then wgt24 = .;
wtgain1= wgt20-wgt16;
wtgain2 = wgt24-wgt20;
wtgainall = wgt24-wgt16;
keep lamb stjul staug stsep lepgjul lepgaug lepgsep wgt16 wgt20 wgt24
    wtgain1 wtgain2 wtgainall year sex dob dage sgroup dgroup litters logepg;

```

```

proc sort;
    by lamb;
run;

```

Filename pedam dde

```

'Excel|J:\Research
Groups\Teladorsagia\Texelmjs\JOanalyses\[RevTexel_Pedigrees.xls]Blythbank!R
2C1:R992C3';

```

```

data ped;
infile pedam missover;
input lamb    $ sire $ dam $;

```

```
proc inbreed data=ped covar outcov=amatrix;

var lamb sire dam;

run;
```

```
data pedigree;

set amatrix;

parm=1;

row=_n_;

run;
```

```
data all;

merge allmhc jjpab weight;

by lamb;

if drb1a = '*' then delete;

if drb1b = '*' then drb1b = drb1a;

if drb1a = '0' then drb1a = ' ';

if drb1b = '0' then drb1b = ' ';

if csrd226a = '0' then csrd226a = ' ';

if csrd226b = '0' then csrd226b = ' ';

if omhc1a = '0' then omhc1a = ' ';

if omhc1b = '0' then omhc1b = ' ';

a224=0;

if drb1a='224' then a224=1;

if drb1b='224' then a224=a224+1;

a228=0;

if drb1a='228' then a228=1;

if drb1b='228' then a228=a228+1;

a530=0;

if drb1a='530' then a530=1;
```

```
if drb1b='530' then a530=a530+1;
a538=0;
if drb1a='538' then a538=1;
if drb1b='538' then a538=a538+1;
a=0;
if drb1a='A' then a=1;
if drb1b='A' then a=a+1;
b1=0;
if drb1a='B1' then b1=1;
if drb1b='B1' then b1=b1+1;
b2=0;
if drb1a='B2' then b2=1;
if drb1b='B2' then b2=b2+1;
c1=0;
if drb1a='C1' then c1=1;
if drb1b='C1' then c1=c1+1;
c2=0;
if drb1a='C2' then c2=1;
if drb1b='C2' then c2=c2+1;
d1=0;
if drb1a='D1' then d1=1;
if drb1b='D1' then d1=d1+1;
d2=0;
if drb1a='D2' then d2=1;
if drb1b='D2' then d2=d2+1;
e=0;
if drb1a='E' then e=1;
if drb1b='E' then e=e+1;
g2=0;
```

```

if drb1a='G2' then g2=1;
if drb1b='G2' then g2=g2+1;
gsf=0;
if drb1a='GSF' then gsf=1;
if drb1b='GSF' then gsf=gsf+1;
h3=0;
if drb1a='H3' then h3=1;
if drb1b='H3' then h3=h3+1;
i=0;
if drb1a='I' then i=1;
if drb1b='I' then i=i+1;
l=0;
if drb1a='L' then l=1;
if drb1b='L' then l=l+1;
m=0;
if drb1a='M' then m=1;
if drb1b='M' then m=m+1;
tuv=0;
if drb1a='TUV' then tuv=1;
if drb1b='TUV' then tuv=tuv+1;
m=0;
if drb1a = '*' then drb1a = ' ';
if drb1a = ' ' then delete;
if tigel4 = . then delete;
hom = 0;
if drb1a=drb1b then hom = 1;
run;
*/
/*

```

```

PROC EXPORT DBMS= EXCELCS

DATA=allmhc

OUTFILE='C:\Users\mjs1z\Documents\texelmhc2.xls' REPLACE;

PORT=9621 ;

SERVER='DELL-8PW5Z4J.campus.gla.ac.uk';

SHEET='MHC';

RUN;

*/

/*

ods trace on;

ods output SolutionF = SF;

***Eight alleles not used because of rarity: a224 a228 a530 a538 b1 c1 d1 e;

proc mixed data=all ;

class lamb dam sire year;

model lepgsep = year dob sex A B2 C2 D2 G2 GSF H3 I L M TUV / solution;

random lamb / type=vc LDATA=pedigree ;

*** random dam(sire);

*** parms (0.12) (0.04) (0.001);

run;


ods trace off;

ods _all_ close;

ods listing;


ods trace on;

ods output SolutionF = SF;

***Eight alleles not used because of rarity: a224 a228 a530 a538 b1 c1 d1 e;

proc mixed data=all ;

class lamb dam sire year;

```



```

model tigel3 = year dob sex A B2 C2 D2 G2 GSF H3 I L M TUV / solution;

random lamb / type=vc LDATA=pedigree ;

random dam(sire);

*** parms (0.12) (0.04) (0.001);

run;

```

```

ods trace off;

ods _all_ close;

ods listing;

```

```

data graph1;

set SF;

if effect = 'Intercept' then delete;

if effect = 'year' then delete;

if effect = 'dob' then delete;

if effect = 'sex' then delete;

if effect = 'dage' then delete;

if effect = 'dgroup' then delete;

if effect = 'sgroup' then delete;

```

```

proc print data=graph1;

run;

```

```

axis1 label = ('IgE L3' font='Times New Roman Symbol') minor = none ;

axis2 value = (angle = 0) label = ('ALLELE' font='Times New Roman Symbol');

```

```

proc gchart data = graph1;

vbar Effect / sumvar = estimate raxis = axis1 descending maxis = axis2;

run;

```

```

proc print;

run;

ods trace on;

ods output SolutionF = SFH;

***Eight alleles not used because of rarity: a224 a228 a530 a538 b1 c1 d1 e;

proc mixed data=all ;

class lamb dam sire year;

model tigel3 = year dob sex hom / solution;

random lamb / type=vc LDATA=pedigree ;

random dam(sire);

*** parms (0.12) (0.04) (0.001);

run;


ods trace off;

ods _all_ close;

ods listing;


data graph1H;

set SFH;

if effect = 'Intercept' then delete;

if effect = 'year' then delete;

if effect = 'dob' then delete;

if effect = 'sex' then delete;

if effect = 'dage' then delete;

if effect = 'dgroup' then delete;

if effect = 'sgroup' then delete;


proc print data=graph1H;

```

```

run;

axis1 label = ('IgE L3' font='Times New Roman Symbol') minor = none ;

axis2 value = (angle = 0) label = ('HOMOZYGOSITY' font='Times New Roman
Symbol');

proc gchart data = graph1H;

vbar Effect / sumvar = estimate raxis = axis1 descending maxis = axis2;

run;

proc print;

run;

ods trace on;

ods output SolutionF = SF2;

***Eight alleles not used because of rarity: a224 a228 a530 a538 b1 c1 d1 e;

proc mixed data=all ;

class lamb dam sire year ;

model igel4g = year sex dob A B2 C2 D2 G2 GSF H3 I L M TUV / solution;

random lamb / type=vc LDATA=pedigree ;

random dam(sire);

*** parms (0.12) (0.04) (0.001);

run;

ods trace off;

ods _all_ close;

ods listing;

data graph2;

```

```

set SF2;

if effect = 'Intercept' then delete;

if effect = 'year' then delete;

if effect = 'dob' then delete;

if effect = 'sex' then delete;

if effect = 'dage' then delete;

if effect = 'dgroup' then delete;

if effect = 'sgroup' then delete;


proc print data=graph2;

run;


axis1 label = ('IgE L4' font='Times New Roman Symbol') minor = none ;
axis2 value = (angle = 0) label = ('ALLELE' font='Times New Roman Symbol');


proc gchart data = graph2;

vbar Effect / sumvar = estimate raxis = axis1 descending maxis = axis2;

run;


proc print;

run;


ods trace on;

ods output SolutionF = SF2H;

***Eight alleles not used because of rarity: a224 a228 a530 a538 b1 c1 d1 e;

proc mixed data=all ;

class lamb dam sire year ;

model igel4g = year sex dob hom / solution;

random lamb / type=vc LDATA=pedigree ;

```

```

random dam(sire);

*** parms (0.12) (0.04) (0.001);

run;


ods trace off;

ods _all_ close;

ods listing;


data graph2H;

set SF2H;

if effect = 'Intercept' then delete;

if effect = 'year' then delete;

if effect = 'dob' then delete;

if effect = 'sex' then delete;

if effect = 'dage' then delete;

if effect = 'dgroup' then delete;

if effect = 'sgroup' then delete;


proc print data=graph2H;

run;


axis1 label = ('IgE L4' font='Times New Roman Symbol') minor = none ;

axis2 value = (angle = 0) label = ('HOMOZYGOSITY' font='Times New Roman
Symbol');


proc gchart data = graph2H;

vbar Effect / sumvar = estimate raxis = axis1 descending maxis = axis2;

run;

```

```

proc print;

run;

ods trace on;

ods output ParameterEstimates = SF3;

***Eight alleles not used because of rarity: a224 a228 a530 a538 b1 c1 d1 e;

proc glimmix data=all ;

class lamb year sex ;

model iga14g = year dob sex A B2 C2 D2 G2 GSF H3 I L M TUV / cl ddfm=kr
dist=gam solution;

random lamb / type=lin(1) LDATA=pedigree;

run;

ods trace off;

ods _all_ close;

ods listing;

data graph3;

set SF3;

if effect = 'Intercept' then delete;

if effect = 'dob' then delete;

if effect = 'sex' then delete;

if effect = 'Scale' then delete;

proc print data=graph3;

run;

axis1 label = ('LogIgA AntiL4');

axis2 label = ('ALLELE');

```

```

proc gchart data = graph3;

vbar Effect / sumvar = estimate raxis = axis1 descending maxis = axis2;

run;


ods trace on;

ods output ParameterEstimates = SF3H;

***Eight alleles not used because of rarity: a224 a228 a530 a538 b1 c1 d1 e;

proc glimmix data=all ;

class lamb year sex ;

model igal4g = year dob sex hom / cl ddfm=kr dist=gam solution;

random lamb / type=lin(1) LDATA=pedigree;

run;


ods trace off;

ods _all_ close;

ods listing;


data graph3H;

set SF3H;

if effect = 'Intercept' then delete;

if effect = 'dob' then delete;

if effect = 'sex' then delete;

if effect = 'Scale' then delete;


proc print data=graph3H;

run;


axis1 label = ('LoglgA AntiL4');

```

```
axis2 label = ('HOMOZYGOSITY');
```

```
proc gchart data = graph3H;
```

```
vbar Effect / sumvar = estimate raxis = axis1 descending maxis = axis2;
```

```
run;
```

```
*/
```

```
/*
```

```
data SF2;
```

```
input number Probt;
```

```
if modz(number, 9) = 0 then delete;
```

```
lnp = log(Probt);
```

```
x = -2*(lnp);
```

```
put obs p lnp x;
```

```
run;
```

```
proc print;
```

```
var number x;
```

```
run;
```

```
proc univariate;
```

```
var x;
```

```
run;
```

```
data metatwo;
```

```
x= 1-probchi(67.33, 100);
```

```
y= 1-probchi(140.21, 112);
```

```
z= 1-probchi(149.75, 126);
```



```
proc print;  
run;  
*/
```

LIST OF REFERENCES

- Adamek, M. et al., 2015. Seven novel HLA alleles reflect different mechanisms involved in the evolution of HLA diversity: Description of the new alleles and review of the literature. *Human Immunology*, 76(1), pp.30–35. Available at: <http://linkinghub.elsevier.com/retrieve/pii/S0198885914005072>.
- Ahmed, A.M. et al., 2015. Breed differences in humoral and cellular responses of lambs to experimental infection with the gastrointestinal nematode *Teladorsagia circumcincta*. *Veterinary Research*, 46(1), pp.1–9. Available at: <http://www.veterinaryresearch.org/content/46/1/8>.
- Akira, M. et al., 1995. Nucleotide sequence and the molecular evolution of a new A2 gene in the DQ subregion of the bovine major histocompatibility complex. *Biochemical and Biophysical Research Communications*.
- Alba-Hurtado, F. et al., 2010. Comparison of parasitological and productive traits of Criollo lambs native to the central Mexican Plateau and Suffolk lambs experimentally infected with *Haemonchus contortus*. *Veterinary parasitology*, 172(3-4), pp.277–82. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20801736> [Accessed December 2, 2014].
- Albers, G. a & Gray, G.D., 1987. Breeding for worm resistance: a perspective. *International journal for parasitology*, 17(2), pp.559–66. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/3294667>.
- Amarante, a F.T. et al., 2009. Resistance of Santa Ines and crossbred ewes to naturally acquired gastrointestinal nematode infections. *Veterinary parasitology*, 165(3-4), pp.273–80. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19656629> [Accessed December 2, 2014].
- Amarante, A.F.T. et al., 2005. Relationship of abomasal histology and parasite-specific immunoglobulin A with the resistance to *Haemonchus contortus* infection in three breeds of sheep. *Veterinary Parasitology*, 128, pp.99–107.
- Amills, M. et al., 2005. Nucleotide sequence and polymorphism of the caprine major histocompatibility complex class II DQA1 (Cahi-DQA1) gene. *Molecular immunology*, 42(3), pp.375–9. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15589326> [Accessed September 22, 2014].
- Amills, M. et al., 2004. Structural characterization of the caprine major histocompatibility complex class II DQB1 (Cahi-DQB1) gene. *Molecular immunology*, 41(9), pp.843–6. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15261455> [Accessed September 17, 2014].
- Amills, M. et al., 1998. The major histocompatibility complex of ruminants. *Revue scientifique et technique (International Office of Epizootics)*, 7(1), pp.108–120.

- Andersson, L. & Rask, L., 1986. Genomic hybridization of bovine class II major histocompatibility genes: 2 . Polymorphism of DR genes and linkage disequilibrium in the DQ-DR region. *Animal genetics*, 17, pp.295–304.
- Apanius, V. et al., 1997. The Nature of Selection on the Major Histocompatibility Complex. *Critical Reviews in Immunology*, 17, pp.179–224.
- Ardlie, K.G., Kruglyak, L. & Seielstad, M., 2002. Patterns of linkage disequilibrium in the human genome. *Nature reviews. Genetics*, 3(4), pp.299–309. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11967554> [Accessed November 27, 2014].
- Atlija, M. et al., 2015. Major Histocompatibility Complex class IIB polymorphism in an ancient Spanish breed. *Immunogenetics*, 67(9), pp.531–537. Available at: <http://link.springer.com/10.1007/s00251-015-0856-z>.
- Ballingall, K.T. et al., 2011. A single nomenclature and associated database for alleles at the major histocompatibility complex class II DRB1 locus of sheep. *Tissue antigens*, 77(6), pp.546–53. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21361877> [Accessed October 12, 2013].
- Ballingall, K.T. et al., 2015. An ancient interlocus recombination increases class II MHC DQA diversity in sheep and other *Bovidae*. *Animal Genetics*, 46(3), pp.333–336. Available at: <http://doi.wiley.com/10.1111/age.12290>.
- Ballingall, K.T. et al., 1998. Identification of diverse BoLA DQA3 genes consistent with non-allelic sequences. *Animal Genetics*, 29(2), pp.123–129.
- Ballingall, K.T., Fardoe, K. & McKeever, D.J., 2008. Genomic organisation and allelic diversity within coding and non-coding regions of the Ovar-DRB1 locus. *Immunogenetics*, 60(2), pp.95–103. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18253728> [Accessed July 30, 2014].
- Ballingall, K.T., Luyai, A. & McKeever, D.J., 1997. Analysis of genetic diversity at the DQA loci in African cattle: evidence for a BoLA-DQA3 locus. *Immunogenetics*, 46, pp.237–244.
- Ballingall, K.T. & Tassi, R., 2010. Sequence-based genotyping of the sheep MHC class II DRB1 locus. *Immunogenetics*, 62(1), pp.31–9. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19943043> [Accessed October 12, 2013].
- Begovich, A.N.N.B. et al., 1992. POLYMORPHISM , RECOMBINATION , AND LINKAGE DISEQUILIBRIUM WITHIN THE HLA CLASS II REGION. *The Journal of Immunology*, 148, pp.249–258.
- Beh, K.J. & Maddox, J.F., 1996. Prospects for development of genetic markers for resistance to gastrointestinal parasite infection in sheep. *International journal for parasitology*, 26(8-9), pp.879–97. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8923137>.
- Bergstrom, T.F. et al., 1998. Recent origin of HLA-DRB1 alleles and implications for human evolution. *Nature genetics*, 18.
- Bishop, S.C. et al., 2011. *Breeding for Disease Resistance in Farm Animals* 3rd ed. S. C. Bishop et al., eds., Oxfordshire, UK: CABI.

- Bishop, S.C. et al., 1996. Genetic parameters for faecal egg count following mixed, natural, predominantly *Ostertagia circumcincta* infection and relationships with live weight in young lambs. *Animal Science*, 63(03), pp.423–428. Available at: http://www.journals.cambridge.org/abstract_S1357729800015319.
- Bishop, S.C. et al., 2004. Genetic parameters for resistance to nematode infections in Texel lambs and their utility in breeding programmes. *Animal Science*, 78, pp.185–194.
- Bishop, S.C. & Stear, M.J., 2000. The use of a gamma-type function to assess the relationship between the number of adult *Teladorsagia circumcincta* and total egg output. *Parasitology*, 121(4), pp.435–440. Available at: http://www.journals.cambridge.org/abstract_S0031182099006526.
- Bisset, S.A. et al., 2001. Breeding sheep in New Zealand that are less reliant on anthelmintics to maintain health and productivity Breeding sheep in New Zealand that are less reliant on anthelmintics to maintain health and productivity. *New Zealand veterinary journal*, 49(6), pp.236–246.
- Bjorkman, P.J. et al., 1987. The foreign antigen binding site and T cell recognition regions of class I histocompatibility antigens. *Nature*, 329.
- Blattman, a N. et al., 1993. A search for associations between major histocompatibility complex restriction fragment length polymorphism bands and resistance to *Haemonchus contortus* infection in sheep. *Animal genetics*, 24(4), pp.277–82. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/7902040>.
- Bot, J. et al., 2004. Association of the MHC with production traits in Merino ewes. *Livestock Production Science*, 86(1-3), pp.85–91. Available at: <http://linkinghub.elsevier.com/retrieve/pii/S0301622603001465> [Accessed December 29, 2014].
- Brown, J., Jardetzky, T.S. & Gorga, J., 1993. Three-dimensional structure of the human class II histocompatibility antigen HLA-DR1. *Nature*, 364.
- Brown, J.H. et al., 1988. A hypothetical model of the foreign antigen binding site of Class II histocompatibility molecules. *Nature*, 332(28).
- Buitkamp, J and Epplen, 1996, 1996. Major histocompatibility and T-cell receptor genes in Artiodactyls : characterization , polymorphism and genetic resistance to a helminthic infection Results and Discussion. , 113, pp.287–291.
- Burke, J.. & Miller, J., 2002. Relative resistance of Dorper crossbred ewes to gastrointestinal nematode infection compared with St. Croix and Katahdin ewes in the southeastern United States. *Veterinary Parasitology*, 109(3-4), pp.265–275. Available at: <http://linkinghub.elsevier.com/retrieve/pii/S0304401702002728>.
- Castillo, J.A.F. et al., 2011. Association between major histocompatibility complex microsatellites, fecal egg count, blood packed cell volume and blood eosinophilia in Pelibuey sheep infected with *Haemonchus contortus*. *Veterinary parasitology*, 177(3-4), pp.339–44. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21208746> [Accessed January 12, 2015].
- Chandrawathani, P. et al., 2002. Nematophagous fungi as a biological control agent

- for nematode parasites of small ruminans in Malaysia: A special emphasis on *Duddingtonia flagrans*. *Veterinary Research*, 33, pp.685–696.
- Chardon, P. et al., 1985. Analysis of the Sheep MHC Using HLA. *Immunogenetics*, 22(349-358), pp.349–358.
- Childers, C.P. et al., 2006. Comparative analysis of the bovine MHC class IIb sequence identifies inversion breakpoints and three unexpected genes. *Animal genetics*, 37(2), pp.121–9. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16573526> [Accessed September 22, 2014].
- Clark, A.G., 2004. The role of haplotypes in candidate gene studies. *Genetic epidemiology*, 27(4), pp.321–33. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15368617> [Accessed October 28, 2014].
- Crawford, D.. et al., 2001. A microsatellite polymorphism in the gamma interferon gene is associated with resistance to gastrointestinal nematodes in a naturally-parasitized population of Soay sheep. *Parasitology*, 122, pp.571–582.
- Crawford, D.C. & Nickerson, D. a, 2005. Definition and clinical importance of haplotypes. *Annual review of medicine*, 56, pp.303–20. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15660514> [Accessed October 20, 2014].
- Dausset, J., 1958. Iso-leuco-anticorps. *Acta Haematol*, 20, pp.156–166.
- Davies, G. et al., 2006. Quantitative trait loci associated with parasitic infection in Scottish blackface sheep. *Heredity*, 96(3), pp.252–8. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16391549> [Accessed October 12, 2013].
- Deverson, E. V et al., 1991. Class II major histocompatibility complex genes of the sheep. *Animal genetics*, 22(3), pp.211–25. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/1928827>.
- Dominik, S., 2005. Quantitative trait loci for internal nematode resistance in sheep: a review. *Genetics, selection, evolution: GSE*, 37 Suppl 1, pp.S83–96. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3226267&tool=pmc-entrez&rendertype=abstract>.
- Donner, H. et al., 2000. MHC diversity in Caucasians, investigated using highly heterogeneous noncoding sequence motifs at the DQB1 locus including a retroviral long terminal repeat element, and its comparison to nonhuman primate homologues. *Immunogenetics*, 51(11), pp.898–904.
- Drudge, J.H., Leland, S.E. & Wyant, Z.N., 1957. Strain Variation in the Response of Sheep Nematodes to the Action of Phenothiazine. *Americna Journal of Veterinary Research*, 18(67).
- Dukkipati, V.S.R. et al., 2006a. ‘ Ovar-Mhc ’ — Ovine major histocompatibility complex: Role in genetic resistance to diseases “ Ovar-Mhc ” – Ovine major histocompatibility complex: *New Zealand veterinary journal*, 54(4), pp.153–160.
- Dukkipati, V.S.R. et al., 2006b. Ovar-Mhc- ovine major histocompatibility complex :

- structure and gene polymorphisms. *Genetics and molecular research*, 5(4), pp.581–608.
- Ellis, S. et al., 2014. Ovine IgA-reactive proteins from *Teladorsagia circumcincta* infective larvae. *International journal for parasitology*, 44(10), pp.743–50. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25004076> [Accessed November 24, 2014].
- Ennen, S. et al., 2009. A field trial to control ovine footrot via vaccination and genetic markers. *Small Ruminant Research*, 86(1-3), pp.22–25. Available at: <http://linkinghub.elsevier.com/retrieve/pii/S0921448809001692> [Accessed December 27, 2014].
- Erlich, H., 2012. HLA DNA typing: past, present, and future. *Tissue antigens*, 80(1), pp.1–11. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22651253> [Accessed March 19, 2014].
- Escayg, a P. et al., 1996. Polymorphism at the ovine major histocompatibility complex class II loci. *Animal genetics*, 27(5), pp.305–12. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8930070>.
- Escayg, A.P. et al., 1997. Association between alleles of the ovine major histocompatibility complex and resistance to footrot. *Research in veterinary science*, (1989), pp.283–287.
- Fabb, S. a et al., 1993. Isolation, characterization and evolution of ovine major histocompatibility complex class II DRA and DQA genes. *Animal genetics*, 24(4), pp.249–55. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/7902039>.
- Feichtlbauer-Huber, P. et al., 2000. Reference-strand-mediated conformation analysis of MHC alleles: a new method for high-resolution typing of the Ovar-DQB genes. *Immunogenetics*, 51(1), pp.65–8. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10663564>.
- Felsenstein, J., 1985. Confidence limits on phylogenies: an approach using the bootstrap. *Evolution*, 39(4), pp.783–791. Available at: <http://www.jstor.org/stable/2408678>.
- Figuerola, F., Günther, E. & Klein, J., 1988. MHC polymorphism pre-dating speciation. *Nature*.
- Forrest, R.H.J. et al., 2010. No evidence for a universal association between variation in faecal egg count for a mixed field-challenge of gastrointestinal parasites and the presence of the Ovar-DQA1 null haplotype in sheep. *Veterinary immunology and immunopathology*, 135(3-4), pp.303–5. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20097431> [Accessed October 12, 2013].
- Fremont, D.H. et al., 1996. Structures of an MHC class II molecule with covalently bound single peptides. *Science (New York, N.Y.)*, 272(5264), pp.1001–4. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8638119>.
- Gao, J. et al., 2010. A complete DNA sequence map of the ovine major histocompatibility complex. *BMC genomics*, 11, p.466. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3091662&tool=pmc>

entrez&rendertype=abstract.

- Gasser, R.B. et al., 2006. Single-strand conformation polymorphism (SSCP) for the analysis of genetic variation. *Nature protocols*, 1(6), pp.3121–8. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17406575> [Accessed May 4, 2014].
- Gelasakis, a. I. et al., 2013. Polymorphism of the MHC-DQA2 gene in the Chios dairy sheep population and its association with footrot. *Livestock Science*, 153(1-3), pp.56–59. Available at: <http://linkinghub.elsevier.com/retrieve/pii/S1871141313001030> [Accessed December 27, 2014].
- Gelhaus, a et al., 1995. Sequence polymorphism of BoLA-DQA. *Immunogenetics*, 42(4), pp.296–298.
- Gibson, J.P. & Bishop, S.C., 2005. Use of molecular markers to enhance resistance of livestock to disease : a global approach Utilising and improving genetic resistance to disease. *Rev . sci. tech. Off. int. Epiz.*, 24(1), pp.343–353.
- Glass, D.N. & Giannini, E.H., 1999. Arthritis & Rheumatism JUVENILE RHEUMATOID ARTHRITIS AS A COMPLEX GENETIC TRAIT. *Arthritis & Rheumatism*, 42(11), pp.2261–2268.
- Glass, E.J., Oliver, R. a. & Russell, G.C., 2000. Duplicated DQ Haplotypes Increase the Complexity of Restriction Element Usage in Cattle. *The Journal of Immunology*, 165(1), pp.134–138. Available at: <http://www.jimmunol.org/cgi/doi/10.4049/jimmunol.165.1.134> [Accessed October 25, 2014].
- González, J.F. et al., 2008. Comparative experimental Haemonchus contortus infectioGonzález, J. F., Hernández, A., Molina, J. M., Fernández, A., Raadsma, H. W., Meeusen, E. N. T., & Piedrafita, D. (2008). Comparative experimental Haemonchus contortus infection of two sheep breeds nat. *Veterinary parasitology*, 153(3-4), pp.374–8. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18394807> [Accessed September 23, 2014].
- Good, B. et al., 2006. Texel sheep are more resistant to natural nematode challenge than Suffolk sheep based on faecal egg count and nematode burden. *Veterinary parasitology*, 136(3-4), pp.317–27. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16414193> [Accessed December 23, 2013].
- Goossens, B. et al., 2000. The susceptibility of Djallonké and Djallonké-Sahelian crossbred sheep to Trypanosoma congolense and helminth infection under different diet levels. *Veterinary parasitology*, 85(1999), pp.25–41.
- Gorer, P.A., 1934. The detection of a Hereditary Antigenic Difference in the Blood of Mice by Means of Human Group A Serum. *Journal of Genetics*, 32(1), pp.17–31.
- Gorer, P.A., Lyman, S. & Snell, G.D., 1948. Studies on the genetic and antigenic basis of tumour transplantation. Linkage between a histocompatibility gene and “fused” in mice. *Proceedings of the Royal Society of London*, 135, pp.499–505.

- Gowane, G.R. et al., 2013. Major histocompatibility complex (MHC) of bovines : an insight into infectious disease resistance. *Livestock Research International*, 1(2), pp.46–57.
- Grain, F. et al., 1993. Restriction fragment length polymorphism of DQB and DRB class II genes of the ovine major histocompatibility complex. *Animal /genetics*, 24, pp.377–384.
- Gray, G.D., 1997. The use of genetically resistant sheep to control nematode parasitism. *Veterinary Parasitology*, 72, pp.345–366.
- Gruner, L. et al., 2003. Experimental infection of Black Belly and INRA 401 straight and crossbred sheep with trichostrongyle nematode parasites. *Veterinary Parasitology*, 116(3), pp.239–249. Available at: <http://linkinghub.elsevier.com/retrieve/pii/S0304401703002954> [Accessed December 2, 2014].
- Gruner, L., Bouix, J. & Brunel, J.C., 2004. High genetic correlation between resistance to *Haemonchus contortus* and to *Trichostrongylus colubriformis* in INRA 401 sheep. *Veterinary parasitology*, 119(1), pp.51–8. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15036576> [Accessed January 6, 2015].
- Gruszczyńska, J. et al., 2005. Restriction fragment length polymorphism of exon 2 Ovar-DRB1 gene in Polish Heath Sheep and Polish Lowland Sheep. *Journal of applied genetics*, 46(3), pp.311–4. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16110189>.
- Gyllensten, U.B., Sundvall, M. & Erlich, H.A., 1991. Allelic diversity is generated by intraexon sequence exchange at the DRBJ locus of primates. *Proceedings of the National Academy of Sciences*, 88(May), pp.3686–3690.
- Hassan, M. et al., 2011. The dynamic influence of the DRB1*1101 allele on the resistance of sheep to experimental *Teladorsagia circumcincta* infection. *Veterinary research*, 42(1), p.46. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3063833&tool=pmc-entrez&rendertype=abstract> [Accessed October 12, 2013].
- Hediger, R., Ansari, H.A. & Stranzinger, G.F., 1991. Chromosome banding and gene localizations support extensive conservation of chromosome structure between cattle and sheep. *Cytogenetic and Genome Research*, 57(2-3), pp.127–134. Available at: <http://www.karger.com/DOI/10.1159/000133131>.
- Herrmann, L.M. et al., 2005. Identification and phylogenetic analysis of 15 MHC class II DRB11 expressed alleles in a ewe-lamb flock. *Immunogenetics*, 57, pp.855–863.
- Herrmann-Hoesing, L.M., White, S.N., Kappmeyer, L.S., et al., 2008. Genomic analysis of *Ovis aries* (Ovar) MHC class IIa loci. *Immunogenetics*, 60(3-4), pp.167–76. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18322680> [Accessed October 12, 2013].
- Herrmann-Hoesing, L.M., White, S.N., Mousel, M.R., et al., 2008. Ovine progressive pneumonia provirus levels associate with breed and Ovar-DRB1. *Immunogenetics*, 60, pp.749–758.

- Hickford, J.G., Ridgway, H.J. & Escayg, a P., 2000. Evolution of the ovine MHC DQA region. *Animal genetics*, 31(3), pp.200–5. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10895311>.
- Hickford, J.G.H. et al., 2004. Diversity of the ovine DQA2 gene. *Journal of animal science*, 82, pp.1553–1563.
- Hickford, J.G.H. et al., 2004. Diversity of the ovine DQA2 gene. *Journal of Animal Science*, 82, pp.1553–1563.
- Hickford, J.G.H., Zhou, H. & Fang, Q., 2007. Haplotype analysis of the DQA genes in sheep: evidence supporting recombination between the loci. *Journal of animal science*, 85(3), pp.577–82. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17121973> [Accessed December 23, 2014].
- Hielscher, a et al., 2006. Heterosis analysis of Haemonchus contortus resistance and production traits in Rhoe sheep, Merino Land sheep and crossbred lambs. *Veterinary parasitology*, 141(3-4), pp.279–84. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16828228> [Accessed December 2, 2014].
- Horton, R. et al., 2004. Gene map of the extended human MHC. *Nature reviews. Genetics*, 5(12), pp.889–99. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15573121> [Accessed January 29, 2014].
- Hoste, H. & Torres-Acosta, J.F.J., 2011. Non chemical control of helminths in ruminants: adapting solutions for changing worms in a changing world. *Veterinary parasitology*, 180(1-2), pp.144–54. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21705144> [Accessed December 17, 2014].
- Hughes, A.L. & Nei, M., 1989. Nucleotide substitution at major histocompatibility complex class II loci : Evidence for overdominant selection. *Proceedings of the National Academy of Sciences*, 86(February), pp.958–962. Available at: <http://www.pnas.org/cgi/content/long/86/3/958> [Accessed September 27, 2014].
- Hui, W. et al., 2012. MHC-DQB1 Variation and Its Association with Resistance or Susceptibility to Cystic Echinococcosis in Chinese Merino Sheep. *Asian-Australasian journal of animal sciences*, 25(12), pp.1660–6. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4094165&tool=pmc-entrez&rendertype=abstract>.
- Hunt, P.W., McEwan, J.C. & Miller, J.E., 2008. Future perspectives for the implementation of genetic markers for parasite resistance in sheep. *Tropical biomedicine*, 25, pp.18–33.
- Huntley, J.F. et al., 2001. Studies on the immunoglobulin E responses to Teladorsagia circumcincta in sheep: purification of a major high molecular weight allergen. *Parasite immunology*, 23(5), pp.227–35. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11309133>.
- Jugo, B.M. & Vicario, a, 2000. Single-strand conformational polymorphism and sequence polymorphism of Mhc-DRB in Latxa and Karrantzar sheep: implications for Caprinae phylogeny. *Immunogenetics*, 51(11), pp.887–97.

Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11003382>.

- Kaminsky, R. et al., 2008. A new class of anthelmintics effective against drug-resistant nematodes. *Nature*, 452(7184), pp.176–80. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18337814> [Accessed December 12, 2013].
- Kaplan, R.M., 2004. Drug resistance in nematodes of veterinary importance: a status report. *Trends in parasitology*, 20(10), pp.477–81. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15363441> [Accessed November 10, 2014].
- Karlsson, L.J. & Greeff, J.C., 2006. Selection response in fecal worm egg counts in the Rylington Merino parasite resistant flock. *Australian Journal of Experimental Agriculture*, 46, pp.809–811.
- Karlsson, L.J.E. & Greeff, J.C., 2012. Genetic aspects of sheep parasitic diseases. *Veterinary Parasitology*, 189, pp.104–112.
- Kauppi, L., 2003. Recombination hotspots rather than population history dominate linkage disequilibrium in the MHC class II region. *Human Molecular Genetics*, 12(1), pp.33–40. Available at: <http://www.hmg.oupjournals.org/cgi/doi/10.1093/hmg/ddg008> [Accessed March 27, 2014].
- Keane, O.M. et al., 2006. Gene expression profiling of naïve sheep genetically resistant and susceptible to gastrointestinal nematodes. *BMC genomics*, 7, p.42. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1450279&tool=pmc-entrez&rendertype=abstract> [Accessed October 12, 2013].
- Keane, O.M. et al., 2007. Transcriptional profiling of *Ovis aries* identifies Ovar-DQA1 allele frequency differences between nematode-resistant and susceptible selection lines. *Physiological genomics*, 30(3), pp.253–61. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17488886> [Accessed October 12, 2013].
- Kelley, J., Walter, L. & Trowsdale, J., 2005. Comparative genomics of major histocompatibility complexes. *Immunogenetics*, 56(10), pp.683–95. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15605248> [Accessed March 20, 2014].
- Kelly, G. a, Kahn, L.P. & Walkden-Brown, S.W., 2013. Measurement of phenotypic resilience to gastro-intestinal nematodes in Merino sheep and association with resistance and production variables. *Veterinary parasitology*, 193(1-3), pp.111–7. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23333138>.
- Kemper, K.E. et al., 2010. Reduction of faecal worm egg count, worm numbers and worm fecundity in sheep selected for worm resistance following artificial infection with *Teladorsagia circumcincta* and *Trichostrongylus colubriformis*. *Veterinary Parasitology*, 171(3-4), pp.238–246.
- Kemper, K.E., Goddard, M.E. & Bishop, S.C., 2013. Adaptation of gastrointestinal nematode parasites to host genotype: single locus simulation models. *Genetics, selection, evolution: GSE*, 45(1), p.14. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3704967&tool=pmc-entrez&rendertype=abstract> [Accessed January 4, 2015].

- Kennedy, M.W., 1989. Genetic control of the immune repertoire in nematode infections. *Parasitology today (Personal ed.)*, 5(10), pp.316–24. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15463137>.
- Kenter, M. et al., 1992. Evolutionary relationships among the primate Mhc-DQA1 and DQA2. *Immunogenetics*, 144, pp.71–78.
- Kimura, M., 1980. A simple method for estimating evolutionary rates of base substitutions through comparative studies of nucleotide sequences. *Journal of molecular evolution*, 16(2), pp.111–120.
- Klein, J., 1987. Origin of major histocompatibility complex polymorphism: the trans-species hypothesis. *Human immunology*, 19(3), pp.155–162.
- Klitz, W. et al., 1995. Discordant Patterns of Linkage Disequilibrium of the Peptide-Transporter Loci within the HLA Class II Region. *American Journal of Human Genetics*, 57, pp.1436–1444.
- Konnai, S. et al., 2003. Sequences and diversity of 17 new Ovar-DRB1 alleles from three breeds of sheep. *European journal of immunogenetics*, 30(4), pp.275–82. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/12919289>.
- Konnai, S. et al., 2003. Technical note: DNA typing for ovine MHC DRB1 using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). *Journal of dairy science*, 86(10), pp.3362–5. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/14594256> [Accessed October 12, 2013].
- Konnai, S. et al., 2003. The Influence of Ovine MHC Class II DRB1 Alleles on Immune Response in Bovine Leukemia Virus Infection. *Microbiology and Immunology*, 47(3), pp.223–232.
- Kostia, S. et al., 1998. Applicability of SSCP analysis for MHC genotyping: fingerprinting of Ovar-DRB1 exon 2 alleles from Finnish and Russian Breeds. *Animal genetics*, 29, pp.453–455.
- Larruskain, A. et al., 2012. Biochemical and Biophysical Research Communications Amino acid signatures in the Ovar -DRB1 peptide-binding pockets are associated with Ovine Pulmonary Adenocarcinoma susceptibility / resistance. *Biochemical and Biophysical Research Communications*, 428(4), pp.463–468. Available at: <http://dx.doi.org/10.1016/j.bbrc.2012.10.085>.
- Larruskain, A. et al., 2010. MHC class II DRB1 gene polymorphism in the pathogenesis of Maedi-Visna and pulmonary adenocarcinoma viral diseases in sheep. *Immunogenetics*, 62(2), pp.75–83. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20049428> [Accessed December 24, 2014].
- Lee, C.Y. et al., 2012. Conserved haplotype blocks within the sheep MHC and low SNP heterozygosity in the Class IIa subregion. *Animal genetics*, 43(4), pp.429–37. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22497756> [Accessed October 12, 2013].
- Lee, C.Y. et al., 2011. The influence of MHC and immunoglobulins A and e on host resistance to gastrointestinal nematodes in sheep. *Journal of Parasitology Research*, 2011.

- Lee, C.Y. et al., 2011. The influence of MHC and immunoglobulins a and e on host resistance to gastrointestinal nematodes in sheep. *Journal of parasitology research*, 2011, p.101848. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3092517&tool=pmc-entrez&rendertype=abstract> [Accessed October 12, 2013].
- Lewontin, R.C., 1964. The interaction of selection and linkage. i. general considerations; heterotic models'. *Genetics*, 49, pp.49–67.
- Li, G. et al., 2012. A physical map of a BAC clone contig covering the entire autosome insertion between ovine MHC Class IIa and IIb. *BMC genomics*, 13(1), p.398. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3475007&tool=pmc-entrez&rendertype=abstract> [Accessed April 25, 2014].
- Little, P.R. et al., 2010. Field efficacy and safety of an oral formulation of the novel combination anthelmintic, derquantel-abamectin, in sheep in New Zealand. *New Zealand veterinary journal*, 58(3), pp.121–9. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3082775&tool=pmc-entrez&rendertype=abstract> [Accessed January 4, 2015].
- Liu, H. et al., 2006. A BAC clone-based physical map of ovine major histocompatibility complex. *Genomics*, 88(1), pp.88–95. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16595171> [Accessed December 7, 2014].
- Lotfi, M. et al., 2012. Polymorphism of Ovar-DRBI second exon with PCR-RFLP technique in Arabi sheep population of Khuzestan province. *Journal of Animal and Veterinary Advances*, 11, pp.760–762.
- MacKinnon, K.M. et al., 2009. Microarray analysis reveals difference in gene expression profiles of hair and wool sheep infected with *Haemonchus contortus*. *Veterinary immunology and immunopathology*, 130(3-4), pp.210–20. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19346008> [Accessed December 2, 2014].
- Matika, O. et al., 2003. Resistance of Sabi and Dorper ewes to gastro-intestinal nematode infections in an African semi-arid environment. *Small Ruminant Research*, 47, pp.95–102.
- McCRIRIE, L. et al., 1997. Heterogeneity in the recognition of *Ostertagia circumcincta* antigens by serum antibody from mature, infected sheep. *Parasite Immunology*, 19(5), pp.235–242. Available at: <http://doi.wiley.com/10.1046/j.1365-3024.1997.d01-202.x> [Accessed January 5, 2015].
- McManus, C. et al., 2014. Selection methods for resistance to and tolerance of helminths in livestock. *Parasite (Paris, France)*, 21, p.56. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25350972> [Accessed November 3, 2014].
- McRae, a. F. et al., 2002. Linkage disequilibrium in domestic sheep. *Genetics*, 160(3), pp.1113–1122.
- Meyer, D. & Thomson, G., 2001. How selection shapes variation of the human major histocompatibility complex: a review. *Annals of human genetics*, 65(Pt 1), pp.1–26. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11415519>.

- Mikko, S. et al., 1997. A Comparative Analysis of Mhc DRB3 Polymorphism in the American Bison (*Bison bison*). *Journal of Heredity*, 88, pp.499–503.
- Mikko, S. et al., 1999. Monomorphism and polymorphism at Mk DRB loci in domestic and wild ruminants. *Immunological reviews*, 167, pp.169–178.
- Miller, J.E. et al., 2006. Segregation of natural and experimental gastrointestinal nematode infection in F2 progeny of susceptible Suffolk and resistant Gulf Coast Native sheep and its usefulness in assessment of genetic variation. *Veterinary parasitology*, 140(1-2), pp.83–9. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16621290> [Accessed December 2, 2014].
- Miller, J.E. & Horohov, D.W., 2006. Immunological aspects of nematode parasite control in sheep. *American Society of Animal Science*, pp.124–132.
- Miltiadou, D. et al., 2005. Haplotype characterization of transcribed ovine major histocompatibility complex (MHC) class I genes. *Immunogenetics*, 57(7), pp.499–509. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16028041> [Accessed May 15, 2014].
- Mitchell, E.S.E. et al., 2010. Anthelmintic resistance on sheep farms in Wales. *The Veterinary record*, 166(21), pp.650–2. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20495166> [Accessed December 27, 2013].
- Mitreva, M. et al., 2007. Parasitic nematodes - from genomes to control. *Veterinary parasitology*, 148(1), pp.31–42. Available at: <http://www.sciencedirect.com/science/article/pii/S0304401707002464> [Accessed March 21, 2014].
- Morris, C.A. et al., 2000. Breeding Sheep in New Zealand for Resistance or Resilience to Nematode Parasites. In R. G.D.Gray, R. Woolaston, & B. D. Eaton, eds. *Breeding for Resistance to Infectious Diseases of Small Ruminants*. Canberra, Australia: ACIAR Monograph, pp. 77–98.
- Morris, R.W. & Kaplan, N.L., 2002. On the Advantage of Haplotype Analysis in the Presence of Multiple Disease Susceptibility Alleles. *Genetic epidemiology*, 233(May), pp.221–233.
- Mugambi, J.M. et al., 1996. Response of Dorper and red Maasai lambs to trickle *Haemonchus contortus* infections. *Research in Veterinary Science*, 61, pp.218–221.
- Murphy, L. et al., 2010. Genetic variation among lambs in peripheral IgE activity against the larval stages of *Teladorsagia circumcincta*. *Parasitology*, 137(8), pp.1249–60. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20233490> [Accessed October 12, 2013].
- Nagaoka, Y. et al., 1999. Ovine MHC Class II DRB1 Alleles Associated with Resistance or Susceptibility to Development of Bovine Leukemia Virus-induced Ovine Lymphoma 1. *American Association for Cancer Research*, pp.975–981.
- National Sheep Association, 2014. *A Vision for British lamb production*, Worchestershire. Available at: http://www.nationalsheep.org.uk/pdf_files/NSANFUVisionDocument28072014

- Nicholas, F.W., 1987. Veterinary genetics / F.W. Nicholas. In *Veterinary genetics*. New York: Oxford University Press,.
- Nieuwhof, G.J. & Bishop, S.C., 2005. Costs of the major endemic diseases of sheep in Great Britain and the potential benefits of reduction in disease impact. *Animal Science*, 81(2003), pp.23–29.
- Nikbakht, G. et al., 2011. Allelic polymorphism in the second exon of Ovar-DRB1 in fat-tailed sheep. *Veterinary journal*, 192(3), pp.547–9. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21945136> [Accessed October 12, 2013].
- Nimbkar, C. et al., 2000. A Comparison of the Growth Performance and Worm Resistance of Lambs Produced by Diallel Crossing of Three Indian Sheep Breeds. *Asian-Australasian Journal of Animal Sciences*, (July), pp.72–75.
- Norimine, J. & Brown, W.C., 2005. Intrahaplotype and interhaplotype pairing of bovine leukocyte antigen DQA and DQB molecules generate functional DQ molecules important for priming CD4(+) T-lymphocyte responses. *Immunogenetics*, 57(10), pp.750–62. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16220347> [Accessed November 5, 2014].
- Ohta, T., 1995. Gene conversion vs point mutation in generating variability at the antigen recognition site of major histocompatibility complex loci. *Journal of Molecular Evolution*, 41(2), pp.115–119. Available at: <http://link.springer.com/10.1007/BF00170662>.
- van Oorschot, R. a et al., 1994. Characterization and evolution of ovine MHC class II DQB sequence polymorphism. *Animal genetics*, 25(6), pp.417–24. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/7695122>.
- Outteridge, P.M. et al., 1996. The PCR typing of MHC-DRB genes in the sheep using primers for an intronic microsatellite: application to nematode parasite resistance. *Immunology and cell biology*, 74(4), pp.330–6. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8872183>.
- Papadopoulos, E., Gallidis, E. & Ptochos, S., 2012. Anthelmintic resistance in sheep in Europe: a selected review. *Veterinary parasitology*, 189(1), pp.85–8. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22503039> [Accessed December 24, 2013].
- Paterson, S., 1998. Evidence for balancing selection at the major histocompatibility complex in a free-living ruminant. *The Journal of heredity*, 89(4), pp.289–94. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9703684>.
- Paterson, S., Wilson, K. & Pemberton, J.M., 1998. Major histocompatibility complex variation associated with juvenile survival and parasite resistance in a large unmanaged ungulate population (*Ovis aries* L .). *Proc National Academic of Sciences*, 95(March), pp.3714–3719.
- Polat, M. et al., 2014. The diversity of major histocompatibility complex class II DRB1 gene in sheep breeds from Xinjiang, China. *Tissue antigens*, (25), pp.1–8. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25430475> [Accessed December 1, 2014].

- Preston, S.J.M. et al., 2014. Current status for gastrointestinal nematode diagnosis in small ruminants: where are we and where are we going? *Journal of immunology research*, 2014(1), p.210350. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4166451&tool=pmc-entrez&rendertype=abstract>.
- Raadsma, H.W., 1998. Breeding for disease resistance in Merino sheep in Australia. *Rev Sci tech*, 7(1), pp.315–328.
- Racioppi, L. et al., 1991. THE MOLECULAR BASIS OF CLASS II MHC ALLELIC CONTROL OF T CELL RESPONSES. *The Journal of Immunology*, 147, pp.3718–3727.
- Rajalingam, R., Cecka, M. & Reed, E.F., 2010. Molecular HLA Typing Methods Used in Clinical Laboratories. In W. Grody et al., eds. *Molecular Diagnostics :Techniques and Applications for the Clinical Laboratory*. London, UK: Elsevier Inc., pp. 367–379. Available at: <http://dx.doi.org/10.1016/B978-0-12-369428-7.00030-6>.
- Rashidi, H. et al., 2013. Genetics of Tolerance and Resistance to Nematode Infection in Sheep H. In *Proceedings, 10th World Congress of Genetics Applied to Livestock Production*.
- Reche, P. a. & Reinherz, E.L., 2003. Sequence Variability Analysis of Human Class I and Class II MHC Molecules: Functional and Structural Correlates of Amino Acid Polymorphisms. *Journal of Molecular Biology*, 331(3), pp.623–641. Available at: <http://linkinghub.elsevier.com/retrieve/pii/S0022283603007502> [Accessed October 29, 2014].
- Rege, J.E.O. et al., 2002. E ffect of breed and season on production and response to infections with gastro-intestinal nematode parasites in sheep in the highlands of Ethiopia. *Livestock Production Science*, 78, pp.159–174.
- Robinson, J. et al., 2013. The IMGT/HLA database. *Nucleic acids research*, 41(Database issue), pp.D1222–7. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3531221&tool=pmc-entrez&rendertype=abstract> [Accessed March 20, 2014].
- Romjali, E. et al., 2000. Peri-parturient rise in faecal strongyle egg counts of different genotypes of sheep in North Sumatra , Indonesia. *Veterinary Parasitology*, 68(1997), pp.191–196.
- Russell, G.C. et al., 1997. Characterization of cattle cDNA sequences from two DQA loci. *Immunogenetics*, 45(6), pp.455–458.
- Saddiqi, H. a et al., 2010. Evaluation of three Pakistani sheep breeds for their natural resistance to artificial infection of *Haemonchus contortus*. *Veterinary parasitology*, 168(1-2), pp.141–5. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19939567> [Accessed December 2, 2014].
- Saddiqi, H. a. et al., 2012. Markers/parameters for the evaluation of natural resistance status of small ruminants against gastrointestinal nematodes. *Animal*, 6(06), pp.994–1004.
- Saitou, N. & Nei, M., 1987. The Neighbor-joining Method: A New Method for

- Reconstructing Phylogenetic Trees'. *Molecular biology and evolution*, 4(4), pp.406–425.
- Sargison, N., 2011. Responsible use of anthelmintics for nematode control in sheep and cattle. *In Practice*, 33, pp.318–327.
- Sargison, N.D. et al., 2007. Observations on the emergence of multiple anthelmintic resistance in sheep flocks in the south-east of Scotland. *Veterinary parasitology*, 145(1-2), pp.65–76. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17134836> [Accessed December 24, 2013].
- Sayers, G., Good, B., Hanrahan, J.P., Ryan, M. & Sweeney, T., 2005. Intron 1 of the interferon gene: Its role in nematode resistance in Suffolk and Texel sheep breeds. *Research in Veterinary Science*, 79, pp.191–196.
- Sayers, G., Good, B., Hanrahan, J.P., Ryan, M., Angles, J.M., et al., 2005. Major Histocompatibility Complex DRB1 gene: its role in nematode resistance in Suffolk and Texel sheep breeds. *Parasitology*, 131(03), p.403. Available at: http://www.journals.cambridge.org/abstract_S0031182005007778 [Accessed September 28, 2013].
- Sayers, G. & Sweeney, T., 2007. Gastrointestinal nematode infection in sheep – a review of the alternatives to anthelmintics in parasite control. *Animal Health Research Reviews*, 6(02), pp.159–171. Available at: http://www.journals.cambridge.org/abstract_S1466252305000101 [Accessed October 12, 2013].
- Schwaiger, F. et al., 1993. The Paradox of MHC-DRB Exon /Intron Evolution : -alpha helix and beta sheet Encoding Regions Diverge While Hypervariable Intronic Simple Repeats Coevolve with beta sheet Codons. *Journal of Molecular Evolution*, 37, pp.260–272.
- Schwaiger, F.W. et al., 1994. Interdependent MHC-DRB exon-plus-intron evolution in artiodactyls. *Molecular biology and evolution*, 11(2), pp.239–249.
- Schwaiger, F.-W. et al., 1995. An ovine Major histocompatibility complex DRB1 allele is associated with low faecal egg counts following natural, predominantly *Ostertagia circumcincta* infection. *International Journal for Parasitology*, 25(7), pp.815–822. Available at: <http://www.sciencedirect.com/science/article/pii/002075199400216B> [Accessed March 21, 2014].
- Schwaiger, F.W. & Epplen, J.T., 1995. Exonic MHC-DRB polymorphisms and intronic simple repeat sequences: Janus' faces of DNA sequence evolution. *Immunological reviews*, 143(143), pp.199–224. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/7558077>.
- Schwieger, F. & Tebbe, C., 1998. A new approach to utilize PCR-single strand-conformation-polymorphism for 16S rRNA gene-based microbial community analysis. *Applied and Environmental Microbiology*, 64(12)(12), pp.4870–4876.
- Scott, P.C. et al., 1991. Nucleotide sequence, polymorphism and evolution of ovine MHC class II DQA genes. *Immunogenetics*, 34(1970), pp.69–79.

- Scott, P.C. et al., 1991. The nucleotide sequence and evolution of ovine MHC class II B genes: DQB and DRB. *Immunogenetics*, 34, pp.80–87.
- Scott, P.C., Choi, C.L. & Brandon, M.R., 1987. Genetic organization of the ovine MHC class II region. *Immunogenetics*, 25(2), pp.116–22. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/3028945>.
- Shen, H. et al., 2014. MHC-DRB1/DQB1 Gene Polymorphism and Its Association with Resistance / Susceptibility to Cystic Echinococcosis in Chinese Merino Sheep. *Journal of Parasitology Reserach*, 2014.
- Sigurdardottir, S. et al., 1992. Gene duplications and sequence polymorphism of bovine class II DQB genes. *Immunogenetics*, 3(205-213), pp.205–213.
- Slatkin, M., 2008. Linkage disequilibrium--understanding the evolutionary past and mapping the medical future. *Nature reviews. Genetics*, 9(6), pp.477–85. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18427557> [Accessed September 17, 2013].
- Snibson, K.J. et al., 1998. Allelic variation of ovine MHC class II DQA1 and DQA2 genes. *Animal genetics*, 29(5), pp.356–62. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9800324>.
- Stear, M.. et al., 1997. The Genetic Basis of Resistance to *Ostertagia circumcincta* in Lambs. *The Veterinary Journal*, 154, pp.111–119.
- Stear, M.J. et al., 1996. An ovine lymphocyte antigen is associated with reduced faecal egg counts in four-month-old lambs following natural, predominantly *Ostertagia circumcincta* infection. *International journal for parasitology*, 26(4), pp.423–8. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8773530>.
- Stear, M.J. et al., 2007. Detection of genes with moderate effects on disease resistance using ovine mhc and resistance to nematodes as an example. *Veterinary immunology and immunopathology*, 120(1-2), pp.3–9. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17765323> [Accessed October 10, 2013].
- Stear, M.J. et al., 2002. Eosinophilia as a marker of resistance to *Teladorsagia circumcincta* in Scottish Blackface lambs. *Parasitology*, 124(Pt 5), pp.553–60. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/12049418>.
- Stear, M.J. et al., 2009. Genetic variation in resistance to mixed, predominantly *Teladorsagia circumcincta* nematode infections of sheep: from heritabilities to gene identification. *Parasite Immunology*, 31(5), pp.274–282. Available at: <http://doi.wiley.com/10.1111/j.1365-3024.2009.01105.x> [Accessed September 17, 2013].
- Stear, M.J. et al., 2007. The dynamic influence of genetic variation on the susceptibility of sheep to gastrointestinal nematode infection. *Journal of the Royal Society, Interface / the Royal Society*, 4(16), pp.767–76. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2394554&tool=pmc_entrez&rendertype=abstract [Accessed January 13, 2015].
- Stear, M.J. et al., 1998. The processes influencing the distribution of parasitic nematodes among naturally infected lambs. *Parasitology*, 117 (Pt 2, pp.165–71. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9778639>.

- Stear, M.J. et al., 1995. The Repeatability of Faecal egg counts, peripheral eosinophil counts, and plasma pepsinogen concentrations during deliberate infection with *ostertagia circumcincta*. *International journal for parasitology*, 25(3), pp.375–380.
- Stear, M.J. et al., 2001. The sustainability, feasibility and desirability of breeding livestock for disease resistance. *Research in veterinary science*, 71(1), pp.1–7. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11666141> [Accessed October 10, 2013].
- Stear, M.J. & Bishop, S.C., 1999. The curvilinear relationship between worm length and fecundity of *Teladorsagia circumcincta*. *International Journal for Parasitology*, 29(5), pp.777–780. Available at: <http://linkinghub.elsevier.com/retrieve/pii/S0020751999000193>.
- Stear, M.J., Doligalska, M. & Donskow-Schmelter, K., 2006. Alternatives to anthelmintics for the control of nematodes in livestock. *Parasitology*, 134(Pt 2), pp.139–51. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17076922> [Accessed March 21, 2014].
- Stear, M.J., Innocent, G.T. & Buitkamp, J., 2005. The evolution and maintenance of polymorphism in the major histocompatibility complex. *Veterinary immunology and immunopathology*, 108(1-2), pp.53–7. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16099055> [Accessed October 10, 2013].
- Stear, M.J. & Murray, M., 1994. Genetic resistance to parasitic disease: particularly of resistance in ruminants to gastrointestinal nematodes. *Veterinary parasitology*, 54(1-3), pp.161–76. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/7846849>.
- Stear, M.J., Singleton, D. & Matthews, L., 2011. An evolutionary perspective on gastrointestinal nematodes of sheep. *Journal of Helminthology*, 85(02), pp.113–120. Available at: http://www.journals.cambridge.org/abstract_S0022149X11000058 [Accessed October 10, 2013].
- Stear, M.J., Strain, S. & Bishop, S.C., 1999. Mechanisms underlying resistance to nematode infection. *International journal for parasitology*, 29(1), pp.51–6; discussion 73–5. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10048819>.
- Stear, M.J. & Wakelin, D., 1998. Genetic Resistance to Parasitic Infection. *Revue scientifique et technique (International Office of Epizootics)*, 17(1), pp.143–153.
- Stefan, T. et al., 2014. The selection forces that maintain diversity at the Major Histocompatibility Complex. *unpublished*.
- Stewart, M. & Miller, R.F., 1938. RESISTANCE OF SHEEP OF DIFFERENT BREEDS TO INFESTATION BY OSTERTAGIA CIRCUMCINCTA. *Journal of Agricultural Research*, 56(12), pp.923–930.
- Takeshima, S. et al., 2007. Establishment of a sequence-based typing system for BoLA-DQA1 exon 2. *Tissue Antigens*, 69(2), pp.189–199.
- Tamura, K. et al., 2013. MEGA6: Molecular evolutionary genetics analysis version 6.0. *Molecular Biology and Evolution*, 30(12), pp.2725–2729.

- Tariq, K. a et al., 2008. Epidemiology of gastrointestinal nematodes of sheep managed under traditional husbandry system in Kashmir valley. *Veterinary parasitology*, 158(1-2), pp.138–43. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18838225> [Accessed December 2, 2014].
- Taylor, M. a. et al., 2009. Multiple resistance to anthelmintics in sheep nematodes and comparison of methods used for their detection. *Small Ruminant Research*, 86(1-3), pp.67–70. Available at: <http://linkinghub.elsevier.com/retrieve/pii/S0921448809001783> [Accessed January 3, 2014].
- Thomson, G. & Single, R.M., 2014. Conditional Asymmetric Linkage Disequilibrium (ALD): Extending the Bi-Allelic r^2 Measure. *Genetics*, 198(September), pp.321–331. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25023400>.
- Tiercy, J. et al., 1989. Remarkable sequence conservation of the HLA-DQB2 locus (DXt3) within the highly polymorphic DQ subregion of the human MHC. *Immunogenetics*, 29, pp.241–248.
- Ting, J.P. et al., 2002. Genetic Control of MHC Class II Expression. *Cell*, 109, pp.21–33.
- Torres-Acosta, J.F.J. & Hoste, H., 2008. Alternative or improved methods to limit gastro-intestinal parasitism in grazing sheep and goats. *Small Ruminant Research*, 77(2-3), pp.159–173. Available at: <http://linkinghub.elsevier.com/retrieve/pii/S0921448808000680> [Accessed December 17, 2014].
- Trowsdale, J. et al., 1993. Genomic structure and function in the MHC HLA-C. *Science*, 9(4), pp.117–122.
- Trowsdale, J., 2011. The MHC, disease and selection. *Immunology letters*, 137(1-2), pp.1–8. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21262263> [Accessed January 3, 2015].
- Ujvari, B. & Belov, K., 2011. Major histocompatibility complex (MHC) markers in conservation biology. *International Journal of Molecular Sciences*, 12(8), pp.5168–5186.
- Urquhart, G.M. et al., 1987. *Veterinary Parasitology*, Avon, UK: Longman Scientific and Technical.
- Valilou, R.H. et al., 2015. Fecal egg counts for gastrointestinal nematodes are associated with a polymorphism in the MHC-DRB1 gene in the Iranian Ghezel sheep breed. *Frontiers in Genetics*, 6(March), pp.1–11. Available at: <http://journal.frontiersin.org/article/10.3389/fgene.2015.00105>.
- Venturina, V.M., 2012. *Relationship between an inflammatory mucosal T cell response and susceptibility of sheep to Teladorsagia circumcincta infection*. University of Edinburgh.
- Venturina, V.M., Gossner, A.G. & Hopkins, J., 2013. The immunology and genetics of resistance of sheep to *Teladorsagia circumcincta*. *Veterinary research communications*, 37(2), pp.171–81. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23430701> [Accessed November 27,

2013].

- Vipond, J.E., 2010. The future of the UK sheep industry. *Royal Agricultural Society of England*, 171, pp.45–48.
- Wakeland, E.K. et al., 1990. Ancestral polymorphisms of MHC class II genes: Divergent allele advantage. *Immunologic Research*, 9(2), pp.115–122.
- Waller, P.J. & Thamsborg, S.M., 2004. Nematode control in “green” ruminant production systems. *Trends in parasitology*, 20(10), pp.493–7. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15363444> [Accessed March 22, 2014].
- Walsh, P.S., Erlich, H. a & Higuchi, R., 1992. Preferential PCR amplification of alleles: Mechanisms and solutions. *Genome Research*, 1(4), pp.241–250.
- Warner, C.M., Meeker, D.L. & Rothschild, M.F., 1987. Genetic Control of Immune Responsiveness: A Review of Its use as a Tool for Selection for Disease Resistance. *Journal of animal science*, pp.394–406.
- Wright, H. & Ballingall, K.T., 1994. Mapping and characterization of the DQ subregion of the ovine MHC. *Animal Genetics*, 25, pp.243–249.
- Zhou, H. & Hickford, J.G.H., 2004. Allelic polymorphism in the dqa1 gene. *Journal of Animal Science*, 82, pp.8–16.
- Zhou, H., Hickford, J.G.H. & Fang, Q., 2005. Polymorphism of the DQA2 gene in goats. *Journal of Animal Science*, 83, pp.963–968.